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THE EFFECT OF RAISED INTRACRANIAL PRESSURE ON THE CEREBRAL BLOOD FLOW

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ONE of the most important conclusions derived from recent work on brain metabolism is the constancy of the cerebral blood supply. This has been clearly shown by Lennox (1936) and Lennox and Leonhardt (1931) in a large group of subjects. Gibbs, Gibbs, and Lennox (1935) have also found that sleep has little effect upon the blood supply of the brain, while Gibbs, Lennox, and Gibbs (1934) have shown that epileptic attacks do not result from a change in the total blood flow. Mental work, however, caused a small increase in the cerebral blood flow, due probably to a dilatation of the cerebral vessels (Lennox and Leonhardt, 1931). The evidence so far seems to indicate that, within limits, a constant rather than a rich supply of oxygen is necessary for the normal functioning of the brain.

The object of the present series of experiments was to ascertain whether increased intracranial pressure, as produced by intracranial tumour, has any effect on this constant cerebral blood flow. It appeared that raised intracranial pressure might possibly exert an effect on the large venous channels, thus causing a partial obstruction to the venous outflow and thereby slowing the cerebral circulation. A series of experiments was first performed on a group of un-anæsthetized human subjects, the results of which indicated that in some cases intracranial tumour did have such a slowing effect. The investigations were then carried further, using cats with artificially produced tumours, in an endeavour to confirm the results obtained in man with neoplastic tumours.

Methods

The cerebral blood flow has been ascertained by measuring the difference in the oxygen and carbon dioxide contents of the blood entering and leaving the brain, the

two samples of blood being taken practically simultaneously. In man the arterial blood was obtained by puncture of the brachial artery and the venous blood by puncture of the jugular bulb. In the cat the arterial blood was obtained from a cannula in the femoral artery and the venous blood from the superior longitudinal sinus, the needle being introduced into this sinus near the anterior part of the brain and passed posteriorly to the torcula, whence the sample was withdrawn. The venous blood obtained in these ways from man and cat should, therefore, be a good representation of the blood coming from the brain as a whole.

The principle of this method of measuring the cerebral blood flow depends upon the amount of oxygen taken up and the amount of carbon dioxide given off as the blood passes through the brain tissue. These amounts will depend upon two factors, first, the rate of metabolism of the brain tissue and, secondly, the volume of blood passing through the brain in a given time. If it is assumed that the rate of the metabolism of the brain remains constant with the patient or animal lying quietly at rest, the arterio-venous differences of oxygen and of carbon dioxide will vary inversely with the volume of blood flowing through the brain in unit time.

All human subjects were unanæsthetized and had been lying at rest in bed for some time before the blood samples were taken. Punctures of the brachial artery and of the jugular bulb were made with the patient lying on his back in a horizontal position. Five c.c. of blood were withdrawn from each puncture and put under paraffin oil without contact with air, coagulation and glycolysis being prevented by 0·2 per cent. potassium oxalate and 0·1 per cent. sodium fluoride respectively. The blood was put on ice and analyses were begun almost immediately. As soon as the blood samples were obtained, the intracranial pressure was measured by ventricular tap or lumbar puncture with the patient still lying in the horizontal position.

All cats were anæsthetized with chloralose (75–80 mgm. per kilogram body weight intravenously), and they were left for 1½ hours after the administration of the anæsthetic before the blood samples were taken. This interval was allowed for the effects of the small amount of ethyl chloride and ether, used before chloralose injection, to wear off. It was found that after this time the arterio-venous oxygen difference remained constant for about 2 hours, but that after 2 hours this difference gradually increased. Thus in all experiments blood samples were taken 1½–2 hours after the chloralose was administered. In this way, constant figures were obtained in normal cats, as will be seen later. The cats were always in the same position, lying horizontally on a table with the head slightly raised and held firmly in a clamp. A narrow longitudinal hole was made in the skull with a dental drill just posterior to the bregma, so that a needle could be passed along the superior longitudinal sinus to the torcula. Blood samples obtained from the sinus and from the femoral artery were dealt with in the same manner as in the case of human subjects described above. The blood pressure was recorded on a drum from a cannula in the femoral artery.

The human subjects with raised intracranial pressure were all suffering from intracranial tumour. In the experiments with cats a group of controls was treated in the way described, while in another group an artificial tumour was introduced into the cranial cavity from 3 to 6 weeks before the blood samples were taken. For the introduction of these artificial tumours, the cat was anæsthetized with nembutal (35 mgm. per kilogram body weight intraperitoneally), a small hole about $\frac{1}{8}$ in. in diameter was made in the skull with a dental drill, and a mass of cotton wool soaked in paraffin wax of a melting point of 50° C. was carefully introduced extradurally with curved forceps. At post mortem it was found that a rounded tumour was in this way produced, causing a marked dent in the brain substance at the site of the tumour. The size of the tumour introduced was always about 0·7 to 1·0 c.c. in volume, the sudden introduction of larger masses than this causing the death of the animal. The tumours were inserted in two positions in two groups of animals, (*a*) in the frontal region just beneath the coronal suture and (*b*) in the cerebellar region beneath the level of the tentorium cerebelli. The two groups of cats were then allowed to recover and

live for three to six weeks, when they were anæsthetized with chloralose and blood samples were removed as already described. No symptoms were observed with the group of cats with frontal " tumours," and in only two of the cats with cerebellar " tumours " were any symptoms noticed. These two cats showed marked ataxia the day after the operation, and this persisted, although it became somewhat less marked. All cats were very well and in excellent condition when the blood samples were taken.

The percentage saturation of the hæmoglobin with oxygen, the oxygen capacity and carbon dioxide content of the blood were determined with the Haldane blood gas apparatus completely immersed in a water bath.

Results

The Effects of Intracranial Tumour on the Cerebral Blood Flow

A. Experiments on Man.—Fig. 1 shows the arterio-venous oxygen differences and the percentage saturation of hæmoglobin in the arterial and jugular blood in 23 cases of intracranial tumour in man. The arterio-venous carbon dioxide differences are practically identical with the oxygen differences, so they are not plotted in the figure. The first column shows the results of the 23 cases as a whole. The mean arterio-venous oxygen difference is 7·6 c.c. per 100 c.c., while the arterio-venous carbon dioxide difference is 7·8 c.c. per 100 c.c. The percentage saturation of the hæmoglobin is 95 in the arterial blood and 54 in the jugular blood. In this series of experiments a group of normal subjects to act as controls has not been investigated. Lennox and Lennox and Leonhardt, however, have investigated a very large series of more or less normal cases, and they find that the arterio-venous oxygen difference is approximately 6·2 c.c. per 100 c.c., while the percentage saturation of the jugular blood is 62. As they find that these values are fairly constant, their figures can be taken for comparison as being average normal values. The average results obtained in 23 cases of intracranial tumour, therefore, show a higher arterio-venous oxygen difference and a lower percentage saturation of the jugular blood than normal. Should the average rate of metabolism of the brain tissue be the same in both groups of cases, then it can be concluded that the cerebral blood flow must be slower in the group of cases with intracranial tumour.

The second and third columns in Fig. 1 show the original group of 23 cases divided into two groups, first, nine cases in which the tumour was situated in the frontal or parietal cortex and, secondly, 13 cases in which the tumour was either in the cerebellum, mid-brain, or in the region of the basal ganglia (four cerebellar tumours, two acoustic tumours, five basal ganglia tumours, and two tumours in the temporal lobe invading the basal ganglia). The situation of the tumour in all cases was confirmed either at operation or post mortem. In the first group of cases the average arterio-venous oxygen difference is 5·8 c.c. per 100 c.c., carbon dioxide difference 6·0 c.c. per 100 c.c., and the percentage saturation of the jugular blood 62. In the second group the arterio-venous oxygen difference is 8·3 c.c. per 100 c.c., carbon dioxide difference 8·5 c.c. per 100 c.c., and the percentage saturation of the jugular blood 51. There is thus a definite difference between these two groups of cases, those with tumours mainly in the frontal or parietal cortex giving results similar to normal, whereas those with tumours in the posterior fossa or in the basal ganglia appear to have

a cerebral circulation that is slower than normal. The intracranial pressure of the first group averaged 280 mm. cerebrospinal fluid, the highest value being 430 mm., while the second group averaged 320 mm. cerebrospinal fluid, the highest value being 520 mm. These pressures were taken with the patient lying in the horizontal position, and are therefore to be regarded as above normal.

One case has not been included in the second and third columns of Fig. 1. This was a case with a meningioma in the region of the occipital cortex. The intracranial pressure was 280 mm. cerebrospinal fluid, the percentage saturation of the arterial blood was 96 and of the jugular blood only 17, giving an arterio-venous oxygen difference of 15·2 c.c. per 100 c.c. and a respiratory quotient of 0·95. The arterio-venous blood sugar difference of 20 mgm. per 100 c.c., corresponded to the arterio-venous oxygen difference of 15·2 c.c., assuming that carbohydrate only was being utilized. In spite of this great difference between the arterial and venous blood the patient felt and appeared to be quite well. A

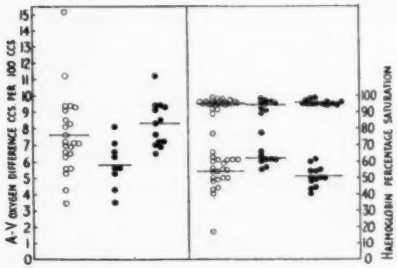

Fig. 1.—The arterio-venous oxygen differences and the percentage saturation of the hæmoglobin of the arterial and jugular blood in a series of 23 cases of intracranial tumour. In the right half of the figure, the upper determinations are for arterial blood and the lower for jugular blood.

○ The group as a whole.
⊙ Cases with tumour in the frontal and parietal regions.
● Cases with tumour in the posterior fossa and basal ganglia.

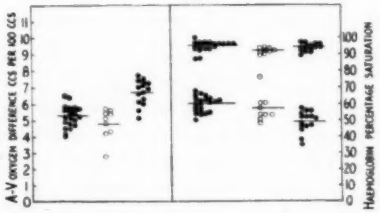

Fig. 2.—The arterio-venous oxygen differences and the percentage saturation of the hæmoglobin of the arterial and jugular blood in cats.

⊙ Group of normal cats.
○ Group of cats with frontal "tumour."
● Group of cats with cerebellar "tumour."

month after the complete removal of the tumour, the hæmoglobin of the jugular blood was 60 per cent. saturated, and the arterio-venous oxygen difference was only 5·5 c.c. per 100 c.c. As the results of this case are so greatly outside the limits observed in the other 22 cases, they have not been included when the group was differentiated, but it appears that the tumour must have exerted some influence on the cerebral blood flow.[1]

B. Experiments on Cats.—Although the two groups of cases above are not very large, it appears that it is the position of the tumour rather than the increased intracranial pressure *per se* which might affect the cerebral blood flow. Because of these results, experiments were performed on cats with the intro-

[1] The detailed results of these experiments in man are shown in Table 1. The letters V and L indicate whether the C.S.F. pressure was ventricular or lumbar.

TABLE 1

	C.S.F. PRESSURE, M.M. C.S.F.	OXYGEN IN BLOOD					CO_2 CONTENT OF BLOOD, VOLS. PER CENT.			RESPIRATORY QUOTIENT
		ARTERIAL		JUGULAR		A–V DIFFERENCE	ARTERIAL	JUGULAR	A–V DIFFERENCE	
		PER CENT. SATURATION	CONTENT	PER CENT. SATURATION	CONTENT					
Cases with posterior fossa or basal ganglia tumours.	V 180	95	15·2	43	6·9	8·3	51·6	60·9	9·3	1·12
	L 420	95	19·8	50	10·4	9·4	54·8	62·0	7·2	0·77
	V 290	99	16·9	44	7·5	9·4	41·5	51·2	9·7	1·03
	V 270	98	17·1	60	10·6	6·5	48·6	54·5	5·9	0·91
	V 215	96	16·6	54	9·4	7·2	59·0	66·7	7·7	1·07
	—	94	18·7	49	9·6	9·1	48·6	57·3	8·7	0·96
	V 520	96	19·5	54	11·0	8·5	51·3	59·8	8·6	1·01
	L 230	97	22·3	48	11·0	11·3	35·8	50·3	14·5	1·27
	L 400	95	19·6	61	12·6	7·0	48·4	55·1	6·7	0·96
	V 350	95	18·0	55	10·4	7·6	51·7	61·1	9·4	1·24
	—	95	16·0	40	6·7	9·3	50·0	59·0	9·0	0·97
	V 300	94	15·0	50	7·9	7·1	62·1	69·5	7·4	1·04
	V 320	95	14·6	50	7·7	6·9	50·6	57·5	6·9	1·00
	320	96	17·6	51	9·3	8·3	50·3	58·8	8·5	1·03
Cases with tumours in the frontal or parietal regions.	V 310	95	15·8	66	10·5	5·3	54·7	60·0	5·3	1·00
	V 430	98	18·8	61	11·7	7·1	52·6	59·6	7·0	0·99
	V 230	95	19·7	56	11·6	8·1	52·1	60·2	8·1	1·00
	L 280	92	18·1	59	11·5	6·6	47·5	54·2	6·7	1·01
	V 220	96	17·5	77	14·0	3·5	60·7	63·7	3·0	0·86
	L 170	91	17·1	63	11·5	5·6	43·0	48·4	5·4	0·97
	V 320	97	14·4	55	8·1	6·3	44·7	53·3	8·6	1·37
	L 300	96	15·1	61	9·5	5·6	53·7	59·6	5·9	1·05
	L 280	89	13·8	61	9·5	4·3	40·6	44·6	4·0	0·93
	280	94	16·7	62	10·9	5·8	50·0	56·0	6·0	1·03

duction of artificial tumours in the frontal and cerebellar regions, as already described in detail. The results of these experiments are shown in Fig. 2. A group of 22 normal cats shows that the average arterio-venous oxygen and carbon dioxide differences are 5·3 c.c. per 100 c.c., while the percentage saturation of the arterial blood is 95 and of the sinus blood 60. The individual figures as shown in Fig. 2 are very constant, with only small variations. The average percentage saturation of the sinus blood, 60, is practically identical with that of normal unanæsthetized human subjects, 62, but the arterio-venous oxygen difference is lower, because the hæmoglobin content of cat's blood is lower than that of human blood, the oxygen capacity in a group of 50 cats being only 14·2 c.c. per 100 c.c.

The arterio-venous oxygen differences of a group of nine cats with frontal " tumour " practically all fall within the limits of the normal group with an average of 4·8 c.c. per 100 c.c., while the arterio-venous oxygen differences of a group of 15 cats with cerebellar " tumours " nearly all fall above the limits of the normal group, with an average of 6·7 c.c. per 100 c.c. The percentage saturations of the arterial and sinus blood in the group of frontal " tumours " are 92 and 57, that is, the same difference as in the normal group. The corresponding figures in the group of cerebellar " tumours " are 94 and 49, the difference in percentage saturation being thus 11 greater than in the normal group. If the average rate of metabolism of the brain tissue is the same in these groups of cats, the blood flow must be slower in the group with cerebellar " tumour " than in the group with frontal " tumour " of the same size or in the normal group.

The blood pressure in all groups of cats was very constant. The average mean arterial blood pressure of the normal group was 124 mm. Hg, frontal " tumour " group 125 mm. Hg, and the cerebellar group 127 mm. Hg, individual variations being between 105 and 140 mm. Hg. The changes observed in the arterio-venous oxygen and carbon dioxide differences in the different groups of cats could therefore not be accounted for by changes in the mean arterial blood pressure.

The effects of the " tumours " in cats on the size of the ventricles can be seen in Fig. 3. In practically all cases the cats with cerebellar " tumours " showed a definite degree of hydrocephalus, whereas those with frontal " tumours " showed no change from normal. Of the 23 human cases described above, the ventricles have been studied by ventriculography in 17 cases, nine from the group with cerebellar or basal ganglia tumours and eight from the group with frontal or parietal tumours. The ventricles in the latter group have a total capacity that is approximately normal, whereas those in the former group are on the whole much increased in size.

The Coefficient of Oxygen Utilization.—Another indication of the differences described is seen in the coefficient of oxygen utilization, that is, the ratio of the oxygen taken up by the tissue to the oxygen available in the arterial blood. Table 2 shows that in the group of human cases with tumours in the frontal or parietal regions, the coefficient of oxygen utilization is 35 per cent., which corresponds closely with the figure of 35·6 per cent. obtained in a group of

normal subjects by Williams and Lennox (1939), and that in the other group of tumours the coefficient of oxygen utilization is 47 per cent. Similarly, in the groups of cats the normal figure of 38 per cent. corresponds with that of 38 per cent. for the frontal " tumour " group, whereas in the group with cerebellar " tumours " the coefficient of oxygen utilization is much higher, 48 per cent. In both groups of human cases and in the three groups of cats the oxygen capacity of the blood is approximately the same (Table 2), although the slightly lower oxygen capacity and percentage saturation of the arterial blood of the group of frontal " tumours " in cats will give the same coefficient of oxygen utilization as normal in spite of the fact that the arterio-venous oxygen difference is lower. On the whole, however, these figures should give a fair indication of the cerebral blood flow. The amount of blood flowing through the brain in any given time will therefore be approximately 30 per cent. less in the case of cerebellar or basal ganglia than in the case of tumours in the frontal or parietal regions or in normals. This change is about the same in the human cases as in the experiments with cats.

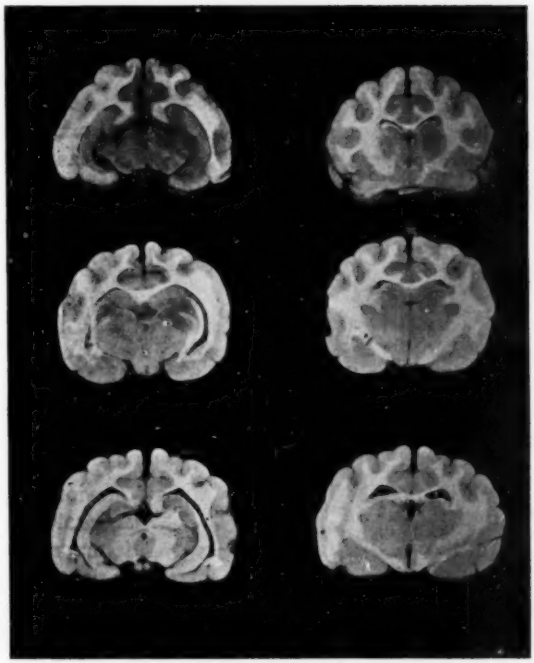

Fig. 3.—Two sections from each of three cats' brains in approximately comparable positions in each, showing the size of the ventricles. (*a*) Normal brain. (*b*) Brain from cat with frontal " tumour." (*c*) Brain from cat with cerebellar " tumour."

TABLE 2

	OXYGEN CAPACITY	OXYGEN IN ARTERIAL BLOOD	OXYGEN IN VENOUS BLOOD	COEFFICIENT OF OXYGEN UTILIZATION
Human subjects: Frontal and parietal tumour group ..	17·4	16·7	10·9	35
Cerebellar and basal ganglia group	18·0	17·6	9·3	47
Cats: Control group	14·6	14·1	8·8	38
Frontal " tumour " group ..	13·5	12·7	7·9	38
Cerebellar " tumour " group ..	14·7	14·1	7·4	48

The Effect of Removal of the Intracranial Tumour in Man.—In five cases the arterio-venous oxygen differences have been measured before operation and from 1 to 3 months after the removal of the intracranial tumour (three total and two subtotal removals), all patients being very well and completely recovered from the operation. The results are shown in Table 3. Although this group is very small, the results indicate that in two cases in which the arterio-venous oxygen difference was normal before operation, no change was observed after operation, whereas in three cases where the arterio-venous oxygen difference was high before operation, a definite fall was observed after operation ; so that the post-operative figures all fall within the range of normality with a mean of 6·3 c.c. per 100 c.c. It seems, therefore, that in those cases with a high oxygen difference, the presence of the intracranial tumour is probably the cause. A larger group of cases is necessary before this can be established with certainty by this method.

TABLE 3.—ARTERIO-VENOUS OXYGEN DIFFERENCE, C.C. PER 100 C.C.

BEFORE OPERATION	AFTER REMOVAL OF TUMOUR
9·4	7·5
8·1	6·3
15·2	5·5
5·3	5·5
6·6	6·5

The Effect of Sudden Rise in Intracranial Pressure in Man.—So far it is the long-standing effects of increased intracranial pressure that have been considered. The effects of a sudden rise in the intracranial pressure have also been investigated. This has been done in six patients who have previously had a cerebellar decompression by removal of a large part of the occipital bone and opening of the dura and in five patients with a subtemporal decompression (three cases) or a small bone defect after removal of a supratentorial tumour (two cases). By pressure on the decompression the intracranial pressure, as measured by a needle in the lateral ventricle, could be raised from normal to 600 or 700 mm. cerebrospinal fluid without causing any inconvenience to the patient. Before pressure was applied, samples of blood were obtained from the jugular bulb and brachial artery in the usual way. While pressure was being applied to the decompression the needle, closed by a stillette, was left in the jugular bulb. After the intracranial pressure had been maintained at about 600 mm. cerebrospinal fluid for approximately 5 minutes, a further sample of jugular blood was

withdrawn. The results are shown in Table 4. In the six cases with cerebellar decompressions, the pressure in each case was raised from approximately normal to 500–700 mm. cerebrospinal fluid and maintained on an average for 5 minutes. In the first three cases there is a marked fall in the percentage saturation of the jugular blood, and a rise in the arterio-venous oxygen difference. The percentage saturation of the jugular blood in these three cases was very low, namely, 26, 22, and 25, yet no signs nor symptoms of this low oxygen saturation were observed. Two cases showed no appreciable difference, while the sixth showed a definite rise in the percentage saturation of the jugular blood and a fall in the arterio-venous oxygen difference. The blood pressure in this last case rose sharply from 140/100 to 160/115 when pressure was applied and fell sharply to the original level when the pressure was released. A third blood sample taken from the jugular bulb 2 minutes after the pressure had been released showed that the percentage saturation and arterio-venous oxygen difference had regained their original levels. The sudden rise in blood pressure, therefore, would account for the sudden increase in the blood flow when the pressure was raised.

TABLE 4

CASE NUMBER	BEFORE PRESSURE APPLIED			DURING PRESSURE ON DECOMPRESSION		
	PER CENT. SATURATION OF JUGULAR BLOOD	A–V O_2 DIFFERENCE	BLOOD PRESSURE	PER CENT. SATURATION OF JUGULAR BLOOD	A–V O_2 DIFFERENCE	BLOOD PRESSURE
CEREBELLAR DECOMPRESSIONS						
N. L. 3915	60	6·5	—	26	11·6	—
E. B. 4015	55	5·9	—	22	10·2	—
A. Y. 4436	50	7·1	130/80	25	11·0	135/90
G. C. 2040	43	8·3	—	42	8·6	—
W. M. 3921.. ..	45	8·5	122/78	48	8·0	126/78
M. M. 3121.. ..	58	5·4	142/100	73	3·1	160/114
	52	7·0	—	40	8·8	—
SUBTEMPORAL DECOMPRESSIONS AND PARIETAL BONY DEFECTS						
E. S. 2579	58	4·7	—	53	5·4	—
C. G. 3968	63	5·4	—	64	5·2	—
N. L. 4363	50	6·9	112/68	51	6·8	118/74
M. B. 4486	40	9·3	120/80	45	8·2	130/92
M. W. 4441.. ..	62	4·3	143/74	62	4·3	166/77
	55	6·1	—	55	6·0	—

The five cases with subtemporal decompressions or with bony defect in the parietal region showed on the whole no change in the cerebral blood flow when pressure was applied to the decompression. The intracranial pressure was not measured in all these cases, but in those cases with subtemporal decompression, where it was measured, the pressure could be raised to 600 mm. cerebrospinal fluid by pressing on the decompression. Thus, though the rise in all cases may not have been as great as in those cases with a cerebellar decompression, because the bony defect was smaller, the intracranial pressure was undoubtedly raised considerably.

Although this series of observations is not large, it appears that when the intracranial pressure is raised by exerting pressure in the temporal or parietal regions, the blood flow is not appreciably affected. Pressure exerted posteriorly at the base of the skull, on the other hand, may in some cases, but not in all, produce a very marked slowing of the cerebral circulation. Three of the cases in this group are interesting in that the percentage saturation of the jugular blood was reduced to 26, 22, and 25 without any inconvenience whatever to the patient. No signs of acute oxygen lack were present and the patients felt quite well. Lennox, Gibbs, and Gibbs (1935) have shown that when the percentage saturation of the jugular blood is suddenly reduced below about 25, unconsciousness takes place. This was certainly not the case with the three patients mentioned above. In another case, described earlier, the percentage saturation of the jugular blood was only 17, and yet the patient was very well and showed no signs of lack of oxygen. It is probable that in this case the percentage saturation was gradually reduced over a long time, but in the three cases described above the change was produced rapidly.

The results of these experiments, on the whole, agree reasonably well with the experiments in cases of long-standing increased intracranial pressure as a result of intracranial tumour. In both series of experiments pressure exerted at the base of the brain posteriorly will in general cause a slowing of the blood flow, whereas pressure exerted in the frontal or parietal regions has little effect.

Discussion

The measurement of the actual volume of blood passing through the brain per minute has met with many difficulties, and an accurate method has not yet been devised. Wolff (1936), Quastel (1939), and Chute and Smyth (1939) review the results so far, and note the great discrepancy between the values for the oxygen uptake per 100 gm. of brain tissue per hour when this is measured *in vivo* and *in vitro*. The values obtained *in vivo* range from 450 to 840 c.c., and *in vitro* from 80 to 300 c.c. If a figure of 600 c.c. oxygen per 100 gm. per hour is applied to the experiments on human subjects described above, assuming a brain of normal size, the cerebral blood flow would be 2·34 litres per minute in the group with tumours in the frontal and parietal regions and 1·65 litres per minute in the group with posterior fossa or basal ganglia tumours. As the total cardiac output in man at rest is only 4–6 litres per minute, it seems unlikely that such a high proportion should pass through the brain. Chute and Smyth find that in the perfused cat's brain the average oxygen consumption is only 200–300 c.c. per 100 gm. per hour, figures which agree more closely with the *in vitro* experiments If a figure of 250 c.c. be applied to the human brain in the present series of experiments, the cerebral circulation would be 980 c.c. per minute in the first group and 683 c.c. per minute in the second group. Similarly, the rate of cerebral blood flow in the cat (assuming an average brain of 30 gm.) would be 24 c.c. per minute in the normal group, 26 c.c. per minute in the group with frontal "tumours," and 19 c.c. per minute in the group with

cerebellar "tumours." These estimates, which are based on the oxygen consumption found in different circumstances (perfused head), may not be applicable to my experiments, but provided the oxygen consumption of the brain per 100 gm. per hour is the same in each group of cases considered, a general idea of the approximate changes in the cerebral blood flow in the different groups of intracranial tumour can be obtained.

Williams and Lennox (1939) have investigated a group of 13 cases suffering from raised intracranial pressure resulting from trauma, tumour, or infection. They find an average arterio-venous oxygen difference of only 6·6 c.c. and a carbon dioxide difference of 6·8 c.c. per 100 c.c., and conclude that raised intracranial pressure has practically no effect on the cerebral blood flow. In my series the figures for the whole group were definitely higher (Fig. 1), and it appears that in certain locations intracranial tumour does have a slowing effect on the blood stream.

It has been suggested that the position of the tumour rather than the actual intracranial pressure, within limits, may account for the changes described. A tumour in the posterior fossa or in the basal ganglia seems more likely to exert a greater effect on the large venous channels which converge at the base of the brain than a tumour in the frontal or parietal cortex. Cairns (1939) has shown that the intracranial pressure is not uniformly distributed throughout the brain in intracranial tumour. The local pressure effects of such a tumour may be much greater than the effects produced in the more remote parts of the cranial cavity. It therefore seems probable that a tumour in the cerebellum, midbrain, or basal ganglia will produce a much greater pressure effect on the large venous channels converging at the base of the brain than will a tumour confined to the frontal or parietal cortex.

It must be remembered that the method of ascertaining the cerebral blood flow which was used in the above series of experiments will give an indication of the total cerebral blood flow only, and not of local changes which may occur in different parts of the brain. It seems quite probable that a tumour in the frontal or parietal cortex will produce local changes in the cerebral circulation, but these changes will not be evident in the arterio-venous oxygen difference of the blood entering and leaving the brain as a whole. Similar changes will no doubt occur locally with tumours of the cerebellum or basal ganglia, but because of the proximity of the large venous channels converging at the jugular foramen, a slowing of the total circulation will be produced, as the results of the series of experiments show.[1]

The rise of venous pressure necessary to bring about the changes described is probably not very great. Bedford (1937) has measured the venous pressure at the torcula in dogs, anæsthetized with ether, after the introduction of artificial subtentorial tumours, and finds no change from normal. This is rather surprising in view of observations at operation with local or general anæsthesia. Cairns (1939) has described how in cases of cerebellar tumours at operation,

[1] Williams and Lennox have shown that in cases with angiomata and vascular tumours the jugular blood has a very high oxygen content. In my series of experiments, however, there is no case of intracranial angioma.

the venous pressure is often greatly increased and bleeding from the veins may be severe. This bleeding may be diminished by lowering the intracranial pressure in these cases, which suggests that the large veins have been partially obstructed. Rise in arterial pressure does not occur until the intracranial pressure approaches the arterial pressure (Cushing, 1901), a figure which is not, or only rarely, observed in cases of intracranial tumour. It is probable that the venous pressure is partly raised by dilatation of the arterioles and capillaries as a result of the rise of carbon dioxide tension caused by the slowing of the blood stream. This would tend to increase the blood flow, but, as the results of my experiments show, this compensatory mechanism cannot totally overcome the obstruction to the large venous channels, and a general slowing of the cerebral circulation results. Thus the raised venous pressure is probably brought about primarily by obstruction to the venous outflow and secondarily by dilatation of the small vessels caused by a rise in the carbon dioxide tension. Further evidence of raised venous pressure is shown in some cases of long-standing increased intracranial pressure by the dilatation of the emissary veins which can be seen in radiographs in the region of the external occipital protuberance. These emissary veins are in direct communication with the large venous sinuses, so it appears that the pressure in these sinuses is raised. Because of the obstruction to the venous outflow at the base of the brain, more blood will therefore escape through these emissary veins.

Summary

The arterio-venous oxygen and carbon dioxide differences of the arterial blood and of the venous blood coming from the brain have been investigated in a group of unanæsthetized human subjects suffering from intracranial tumour, and in cats in which artificial tumours had been inserted extradurally in the frontal and cerebellar regions about 3–6 weeks previously.

The arterio-venous blood gas differences indicated that an intracranial tumour produced a slowing of the cerebral circulation in some cases. An attempt to differentiate the group on the basis of the position of the tumour has been made. With moderate increase in intracranial pressure, tumours in the frontal or parietal regions have little effect on the total cerebral circulation, whereas tumours in the cerebellum or basal ganglia have a slowing effect. This applies to the experiments with cats as well as with man.

The difference observed in the two cases is explained by the local pressure effects of the tumour, a tumour at the base of the brain having a greater influence on the large venous channels as they converge towards the base of the skull than a tumour in the frontal or parietal cortex.

In a small group of cases, removal of the tumour in man has reduced the arterio-venous oxygen difference to normal where this was previously high.

A sudden large rise of intracranial pressure in man by mechanical pressure on a bony defect over the cerebellum, produced for decompression, showed a marked slowing of the cerebral circulation in some cases, whereas a similar rise of pressure caused by mechanical pressure in the fronto-temporal or parietal regions showed no change.

I am greatly indebted to Prof. Hugh Cairns for his help and for the facilities provided in carrying out this work.

REFERENCES

Bedford, T. H. B. (1937). *Brain*, **60**, 211.
Cairns, H. (1939). *Brit. J. Surg.*, **27**, 275.
Cushing, H. (1901). *Bull. Johns Hopk. Hosp.*, **12**, 290.
Chute, A. L., and Smyth, D. H. (1939). *Quart. J. exp. Physiol.*, **29**, 379.
Gibbs, F. A., Gibbs, E. L., and Lennox, W. G. (1935). *Brain*, **58**, 44.
Gibbs, F. A., Lennox, W. G., and Gibbs, E. L. (1934). *Arch. Neurol. Psychiat., Chicago*, **32**, 257.
Lennox, W. G. (1936). *Arch. Neurol. Psychiat., Chicago*, **36**, 375.
Lennox, W. G., Gibbs, F. A., and Gibbs, E. L. (1935). *Ibid.*, **34**, 1001.
Lennox, W. G., and Leonhardt, E. (1931). *Ibid.*, **26**, 719.
—— (1931). *Ibid.*, **26**, 725.
Quastel, J. H. (1939). *Physiol. Rev.*, **19**, 135.
Williams, D., and Lennox, W. G. (1939). *Quart. J. Med.*, **32**, 185.
Wolff, H. G. (1936). *Physiol. Rev.*, **16**, 545.

THE METABOLISM OF THE BRAIN

BY

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IN a previous paper (Courtice, 1940) observations on the cerebral circulation in unanæsthetized subjects suffering from intracranial tumour and in cats anæsthetized with chloralose have been reported. In these experiments the arterio-venous carbon dioxide and oxygen differences have been measured with the subjects and animals lying quietly at rest, so that the respiratory quotients may be calculated, thereby giving an indication of the metabolism of the brain tissue. The methods employed have already been described in detail. The blood sugar estimations given below were made by the method of Hagedorn and Jensen (Peters and van Slyke, 1932), each determination being done in triplicate.

In Fig. 1 are plotted the arterio-venous carbon dioxide differences against

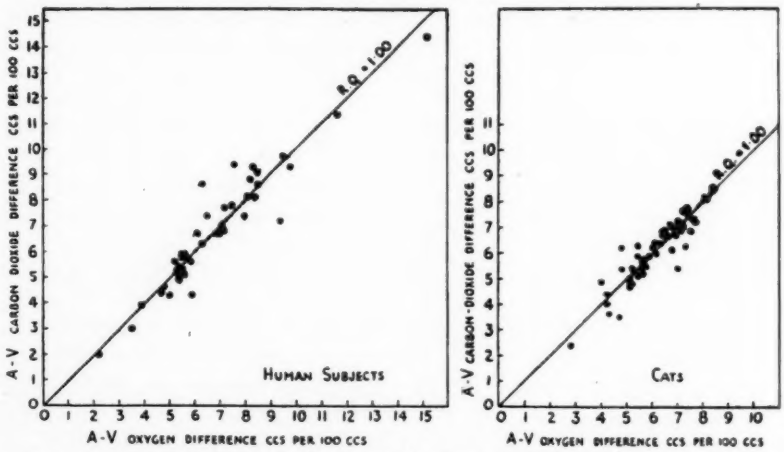
A-V CARBON DIOXIDE DIFFERENCE CCS PER 100 CCS
R.Q. = 1.00
HUMAN SUBJECTS
A-V OXYGEN DIFFERENCE CCS PER 100 CCS
A-V CARBON-DIOXIDE DIFFERENCE CCS PER 100 CCS
R.Q. = 1.00
CATS
A-V OXYGEN DIFFERENCE CCS PER 100 CCS

Fig. 1.—The relation between the carbon dioxide given off and the oxygen taken up by the brain, in unanæsthetized human subjects and in cats.

the arterio-venous oxygen differences in a series of human subjects (43 determinations on 30 subjects, some of whom were not suffering from intracranial tumour and had a normal intracranial pressure), and in a series of cats (50 in

number). It can be seen from these observations that practically all the points lie very close to a line representing a respiratory quotient (that is, the ratio of the carbon dioxide given off to the oxygen taken up, expressed in volumes) of unity. Of the human cases 35 and of the cats 41 determinations lie within the range of 0·90 to 1·10. All the cats and the majority of human cases were without food for 12 to 18 hours, the remainder of the latter being without food for several hours.

The method of measuring the carbon dioxide given off and of the oxygen taken up by the brain tissue will be true only if the blood is neither concentrated nor diluted in its passage through the capillaries, that is, if the volume of blood entering is the same as that leaving the brain in a given time. Should there be any change in the volume of blood plasma as it passes through the brain, the hæmoglobin concentration will vary accordingly. In all samples of blood taken the oxygen capacity has been measured, and the average results of these measurements are shown in Table 1. These average figures show that there is practically no difference between the hæmoglobin concentration of the blood entering and leaving the brain, while in each individual case the difference has likewise been negligible. Thus no error has been incurred by concentration or dilution of the blood in its passage through the brain tissue. Since the subjects and the animals were lying quietly at rest while the blood samples were being taken and for a considerable time before, there should be no disturbance of the acid-base balance of the blood which would upset the respiratory quotient, so that the ratio of the arterio-venous carbon dioxide difference to the arterio-venous oxygen difference should give a true indication of the foodstuffs utilized by the brain.

TABLE 1

	OXYGEN CAPACITY, C.CS. PER 100 C.CS.	
	ARTERIAL BLOOD	VENOUS BLOOD
Human Subjects: average of 43 cases	17·0	17·2
Cats: average of 50 cases	14·4	14·4

The average respiratory quotients of the groups of human subjects and of cats, depicted in Fig. 1, as well as of the smaller groups which were discussed in the previous paper, are shown in Table 2. In both groups, in human subjects and in cats, the average respiratory quotient is 1·00, which indicates that the brain is utilizing carbohydrate only, in spite of the fact that the majority of cases were without food for a considerable time, and presumably had a total respiratory quotient for the whole body of approximately 0·80 to 0·85.

That this respiratory quotient of unity really indicates the utilization of carbohydrate only has been further shown in a small group of cases, both in human subjects and in cats, by measuring the arterio-venous blood sugar differences together with the arterio-venous carbon dioxide and oxygen

differences. The results are shown in Table 3. It can be seen that on the average the actual blood sugar difference is equal to the theoretical blood sugar difference, assuming that carbohydrate only is being used, in a group of ten cats, and almost so in a group of ten human subjects. In both groups the mean respiratory quotient is approximately unity. In one subject in whom the percentage saturation of the jugular blood was only 17 and the arterio-venous oxygen difference 15·2 c.c. per 100 c.c., it is interesting to note that the blood sugar difference was 20 mgm. per 100 c.c. and agreed exactly with the theoretical value.

TABLE 2

	A–V CO_2 DIFFERENCE, C.C. PER CENT.	A–V O_2 DIFFERENCE, C.C. PER CENT.	RESPIRATORY QUOTIENT
Human subjects:			
All cases (43)	6·9	6·9	1·00
Frontal and parietal tumours (9) ..	6·0	5·8	1·03
Other tumours (13)	8·5	8·3	1·03
Cats:			
All cases (50)	6·0	6·0	1·00
Controls (22)	5·3	5·3	1·00
Frontal " tumours " (9)	5·0	4·8	1·04
Cerebellar " tumours " (15)	6·5	6·7	0·97

TABLE 3

	RESPIRATORY QUOTIENT	A–V O_2 DIFFERENCE	THEORETICAL A–V B.S. DIFFERENCE	ACTUAL A–V B.S. DIFFERENCE
Human subjects	0·96	5·5	7	9
	0·91	6·5	9	7
	0·98	11·6	16	13
	1·07	7·2	10	8
	1·01	6·6	9	5
	1·34	8·2	11	12
	1·01	8·5	10	8
	0·99	7·1	9	10
	0·77	9·4	13	12
	0·95	15·2	20	20
	1·00	8·6	11·4	10·4
Cats	0·96	7·6	10	10
	1·05	6·1	8	8
	1·03	6·0	8	4
	0·98	6·1	8	9
	0·97	7·2	10	8
	1·02	6·3	8	9
	0·98	7·1	10	11
	1·06	6·7	9	10
	0·98	5·0	7	7
	1·05	5·3	7	9
	1·01	6·3	8·5	8·5

The comparison of the respiratory quotient of the brain with other parts of the body has been made by Lennox and Leonhardt (1931) in a large series of experiments. In the present series of experiments investigations of three subjects only have been made to show that similar results are obtained by the Haldane blood gas apparatus as by the van Slyke apparatus used by most other observers. Table 4 shows the results in three human subjects of the respiratory quotients and of the arterio-venous oxygen differences, samples being taken from the brain and arm simultaneously. In these cases the respiratory quotient of the brain is approximately unity, while that of the arm is 0·81. The theoretical blood sugar differences in two cases corresponding to these respiratory quotients and oxygen differences agree very well with the blood sugar differences actually measured. The theoretical blood sugar differences in the two observations on the metabolism of the arm have been calculated from the proportions of fat and carbohydrate used assuming that the respiratory quotient is a true indication of the foodstuffs utilized.

TABLE 4

	RESPIRATORY QUOTIENT	A–V O_2 DIFFERENCE	THEORETICAL A–V B.S. DIFFERENCE	ACTUAL A–V B.S. DIFFERENCE
Jugular vein:				
(*a*)	1·07	7·2	10	8
(*b*)	1·03	8·2	11	12
(*c*)	1·08	5·2	—	—
Antecubital vein:				
(*a*)	0·84	7·6	4	4
(*b*)	0·84	13·5	7	6
(*c*)	0·75	4·9	—	—

Discussion

The results described indicate that the methods employed give an accurate indication of the metabolism of the brain tissue. Previous investigations of the respiratory quotient of the brain *in vivo*, estimated by measuring the oxygen and carbon dioxide content of the blood entering and leaving the brain, have varied somewhat, but on the whole they have shown that the brain utilizes mainly carbohydrate. Lennox (1930) found in a series of fifty-one human subjects an average respiratory quotient of 0·90, but in later investigations Lennox and Leonhardt (1931) found in a series of 120 cases an average respiratory quotient of 0·95, and they conclude that the results of this series are probably more correct than the first. More recently, Williams and Lennox (1939) found in four groups of subjects average respiratory quotients varying from 0·94 to 1·10, although their individual results varied within the wide range of 0·05 to 2·66. In a small group of anæsthetized dogs, both normal and diabetic, Himwich and Nahum (1932) have shown that the respiratory quotient is 1·00.

Lennox and Leonhardt (1931) have also measured the arterio-venous blood sugar differences in some of their subjects and find that the difference is much greater in the brain than in the arm and leg. They point out, however, that the arterio-venous oxygen difference of the brain is also greater than that of the arm and leg, and conclude that for this reason they are unable to relate the high utilization of sugar by the brain with its high respiratory quotient. In their table of results they do not correlate the arterio-venous oxygen and blood sugar differences, but only give average oxygen and carbon dioxide values in a large group of cases and average blood sugar values for a much smaller group of cases. It is therefore impossible to say from their figures how closely the utilization of sugar agrees with the respiratory quotient.

Chute and Smyth (1939), using the isolated perfused cat's brain, find that the theoretical oxygen consumption required for the disappearance of glucose is less than the actual oxygen consumption. It would appear, therefore, that the brain is using in these circumstances substances other than glucose.

The results of the present series of experiments show that the respiratory quotient of the brain is very constant and approximately unity in all cases. The determinations of the blood sugars taken in correlation with the respiratory quotients and arterio-venous oxygen differences indicate that the brain is utilizing carbohydrate almost entirely.

References

Chute, A. L., and Smyth, D. H. (1939). *Quart. J. exp. Physiol.*, **29**, 379.
Courtice, F. C. (1940). *J. Neurol. Psychiat.*, **3**, 293.
Himwich, H. E., and Nahum, L. H. (1932). *Amer. J. Physiol.*, **101**, 446.
Lennox, W. G. (1930). *Arch. intern. Med.*, **46**, 630.
Lennox, W. G., and Leonhardt, E. (1931). *Arch. Neurol. Psychiat., Chicago*, **26**, 719.
Peters, J. P., and van Slyke, D. D. (1932). *Quantitative Clinical Chemistry*, vol. 2, Baillière, Tindall and Cox, London.
Williams, D., and Lennox, W. G. (1939). *Quart. J. Med.*, **32**, 185.

CEREBELLAR ATROPHY ASSOCIATED WITH ÉTAT MARBRÉ OF THE BASAL GANGLIA

BY

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THIS paper records the occurrence in a 33-year-old idiot of bilateral état marbré of caudate nucleus, putamen, and thalamus, together with a small atrophic cerebellum, atrophied inferior olives, and sclerosis of the nuclei pontis and the transverse pontine fibres. This combination of lesions is surprising since état marbré of the corpus striatum is in the large majority of cases a phenomenon of infancy (Scholz *et alia*, 1938) and olivo-ponto-cerebellar atrophy is in general a disease of the sixth or fifth decades. A search of the literature concerning the former condition has failed to reveal its association with systematic cerebellar atrophy, although small foci of degeneration in the cerebellum may be found in cases of striatal état marbré, especially when the cerebral cortex is involved and epilepsy present. On the other hand, it is well known that symptoms referable to disease of the extrapyramidal motor system may complicate olivo-ponto-cerebellar atrophy. Among several cases may be mentioned the examples recorded by Guillain and co-workers (1926) in which Parkinsonian rigidity and tremor were observed, and the case of Van Bogaert and Bertrand (1930) in which there was tremor without rigidity. Pathological confirmation of extrapyramidal lesions of a more conclusive character than the above-mentioned observers were able to furnish was provided by Scherer (1933), who in four cases of olivo-ponto-cerebellar atrophy demonstrated well-defined lesions in the substantia nigra and putamen. État marbré was not observed. It would seem that the present case, although having affinities with these adult conditions, differs from them in several respects, notably in the early onset of the pathological process. Another peculiar feature is the absence of clinical signs suggestive either of extrapyramidal or cerebellar disease. For these reasons I have thought it worthy of record.

Case Record

The patient, a male idiot, was admitted to Stoke Park Colony when 8 years old. The records state that he began to walk at the age of 1 year 9 months and that signs of mental deficiency were first observed at the end of the first year.

Family History.—The father earned his living for about 20 years as a corporation roadsweeper. He was certified as a lunatic in 1922 owing to mental depression and

delusions of persecution. He was discharged after 2 years. In 1938 he had a stroke and died after a second attack in 1940.

The mother, aged 73, is mentally normal. The home is well cared for. The patient was the third of a family of four. The eldest sister is married; she had had a healthy illegitimate child. The next sister, who works in a corset factory, has two healthy children. She was on probation for two years for theft. The youngest sister, also married, but with no children, does daily work. This family history, though perhaps indicative of moral shortcoming, provides no evidence of inherited nervous disease.

On admission he was classified as an idiot with mental age under 3 years. Speech was limited to noises. He did not suffer from epilepsy. There was imperfect control of bladder and rectum. No abnormality in the various physical systems was discovered. In 1933, when 27 years old, his performance in the Merrill-Palmer scale of tests indicated a mental age of 2 years 3 months. Considering the idiot level of his achievement, the detailed report of these tests did not indicate a special failure in tasks requiring motor co-ordination. Thus he was able to build a tower of nine blocks, could stand on one foot and put pegs into the Wallin Peg Board B in 21 seconds (3–3½ year level). His failures could be ascribed to general intellectual defect rather than to specific physical handicap.

A physical examination made at this time showed considerable retardation in development. Head length: 175 mm., head breadth 142 mm., head height 120 mm. The calculated capacity of skull was 1,195 c.mm. (about the 7th year level). Standing stature 1,469 mm. (14-year level); sitting stature: 797 mm. (15 year level); weight 39·4 kilos (14-year level). The only abnormality noted in the nervous system was spasticity in the lower limbs. In 1935 he developed acute nephritis, making a good recovery. In 1937 he was critically ill with diphtheria and remained in hospital for four months. The spasticity in the legs increased after this illness. At no time was athetosis, tremor, Parkinsonian rigidity, or inco-ordination of cerebellar type observed. He was described by the nurses who had charge of him as a very timid boy, and he had two characteristic tricks which consisted of pointing upwards with extended index finger and licking his lips with a circular movement of a very long tongue. In 1939 at the age of 33 years he died from broncho-pneumonia.

Post Mortem Report

Lungs: purulent bronchiolitis with small patches of lobular consolidation. Microscopic examination showed a lipoid pneumonia of long standing, with a superimposed terminal hæmorrhagic broncho-pneumonia of influenzal type. Heart: normal save for a few subepicardial petechiæ. Kidneys: macroscopically and microscopically showed a moderate degree of fibrosis. Adrenals were healthy. Liver: showed fatty changes. Spleen: was moderately enlarged, soft, pulpy. Skull: was abnormally convex in the temporal regions, there being no depressions beneath the temporal muscles. The sphenoidal sinus contained a mucopurulent exudate.

Brain.—On removing the dura the cerebral convolutions were found to be somewhat flattened. The brain as a whole was small. There was a purulent meningitis in places at the base of the brain and a localized purulent exudate in the pituitary fossa.

On stripping the leptomeninges the convolutional pattern showed no gross departure from normal. The right calcarine fissure was short and indented the convex border of the hemisphere rather high up on the occipital lobe. The cerebellum (Figs. 1, 2) was grossly reduced in size, the reduction chiefly affecting the lateral lobes in symmetrical fashion, the vermis being unduly visible. Viewed from the side it was seen that the white matter was exposed owing to the poor development of the cerebellar gyri of the superior and inferior surfaces (Fig. 3). The sulci of the lateral lobes were widened, chiefly in the posterior and lateral part of the cerebellum (superior and inferior semilunar lobules) and the consistency was increased in this situation, suggesting glial sclerosis. The pons and medulla were not obviously reduced in size

(when compared with the brain as a whole). Total brain weight (stripped): 1,151 grm.; right hemisphere: 541 grm.; left hemisphere: 546 grm.; cerebellum with pons and medulla: 64 grm. Brain, length: 158 mm.; breadth: 124 mm.; height: 105 mm.

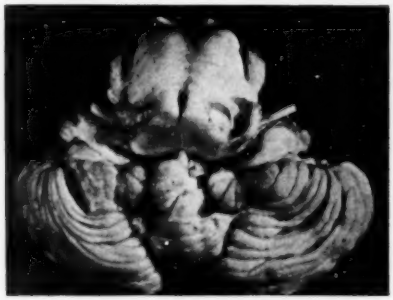

Fig. 1.—Ventral surface of cerebellum showing small size of lateral lobes the sulci of which are widened. $\frac{2}{3}$ natural size.

Fig. 2.—Dorsal surface of cerebellum. $\frac{2}{3}$ natural size.

Fig. 3.—Right lateral lobe of cerebellum viewed from side showing exposure of central white matter. Natural size.

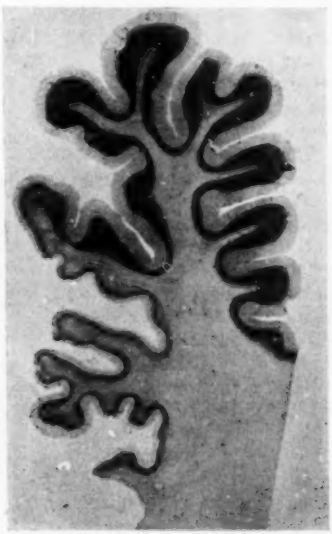

Fig. 4.—Part of the inferior semilunar lobule showing varying degrees of atrophy. The Purkinje cells are almost absent from the better preserved folia. Cresyl violet ; ×5.

Microscopical Examination of the Nervous System

Cerebellum.—Sections were prepared from representative areas of the vermis and lateral lobes (chiefly on the left side) and stained by standard methods for nerve cells, axis cylinders, glia, and myelin.

Lateral lobes: the most marked pathological changes were found in the macroscopically atrophied semilunar lobules. Both sides were equally affected. In the shrunken gyri there was an almost complete absence of Purkinje cells, the granular layer being thinned, but seldom totally atrophied (Fig. 4). The remaining Purkinje cells had a shrunken atrophic appearance. Empty basket fibres of coarse calibre were a conspicuous feature of such areas (Fig. 5). Axonal torpedoes were only rarely seen. There was considerable diminution in the number of myelinated fibres present in the granular layer, but the central core of white matter showed but little thinning even in the atrophic gyri. The molecular layer was thin in the gyri showing marked outfall of Purkinje cells. The tangential fibres were well preserved. There was a heavy fibrillary gliosis affecting the Bergmann glia of the molecular layer (Fig. 6), and also the central white matter in the atrophic gyri. Gliosis was not marked in the granular layer except in those areas where gross reduction in numbers of nerve cells was present.

These pathological changes varied considerably in different parts of the cerebellum. In the macroscopically less affected parts of the semilunar lobules (adjoining the vermis) and in the posterior quadrangular lobule the Purkinje cell loss was not so severe, and the granular layer was well preserved. Empty basket fibres were common. The size of the Purkinje cells varied, many small forms being seen. In such areas the molecular layer was of normal depth and only an occasional thickened Bergmann fibril could be demonstrated. A mild fibrillary gliosis was usually present in the granular layer. In the white matter of the folia, however, excess of fibrous glia was the rule. The myelin picture in these less atrophic regions differed little from normal. In one section taken from the less shrunken part of the right superior semilunar lobule a large cluster of heterotopic Purkinje cells with attendant basket fibres was seen in a malformed folium. In the anterior part of the quadrangular lobules no pathological changes could be found.

The left tonsil showed some reduction in Purkinje cells and coincident empty baskets. Small poorly staining Purkinje cells were common. The intensity of the atrophic changes varied considerably from folium to folium. In general the myelin picture was normal. There was a well-marked fibrillary gliosis in the white matter, but the molecular layer seemed unaffected and was of normal depth.

In the left flocculus there was some thinning and beading of the myelinated fibres in the granular layer. The nerve cell loss was insignificant. There was gliosis of the white matter.

Vermis: in the superior vermis only mild changes were present. Clusters or reduplication of Purkinje cells were occasionally seen. Rarely, gaps in the Purkinje cell layer were present, but empty basket fibres were unusual. Apart from a heavy fibrillary gliosis of the white matter, little abnormal was seen. There was no demyelination. Similar findings were recorded in the inferior vermis. The Purkinje cells varied in size both in cresyl violet and Bielschowsky preparations. In the pyramid empty basket fibres were fairly common. As elsewhere, the white matter was sclerosed without any evidence of corresponding myelin defect. No axonal torpedoes were seen in any part of the vermis.

Dentate nucleus: a few areas devoid of nerve cells were found. In general, however, the nerve cells and their processes appeared healthy. Lipochrome deposits were present to an extent equal to that found in a normal adult. The fibrous gliosis, present throughout the white matter of the cerebellum, was intensified round the cells of the dentate nucleus, especially so in the areas of nerve cell atrophy.

Cerebral Cortex.—Representative areas including the Rolandic areas and cornu Ammonis were examined from both hemispheres. Apart from minor irregularities in arrangement and size of cell commonly seen in low-grade defectives little abnormality was detected. No atrophic changes were found in the many areas examined. A mild fibrillary gliosis was seen in the white matter of the calcarine area and in the fimbria and dorsal part of dentate gyrus of the hippocampus.

Fig. 5.—Empty basket fibres in folium showing well preserved granular layer. Bielschowsky's stain; ×180.

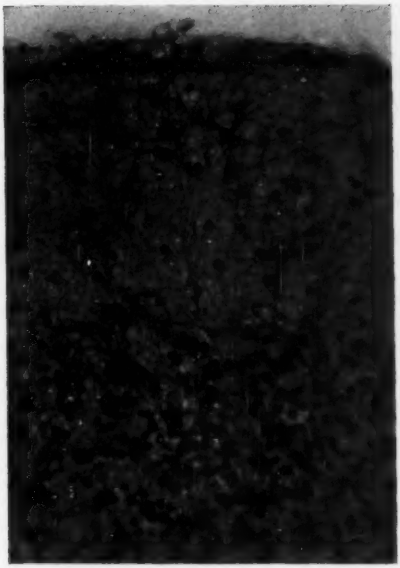

Fig. 6.—Heavy fibrillary gliosis in molecular and granular layers of cerebellum. Holzer stain; ×270.

Fig. 7.—Coronal section through right corpus striatum. État marbré in caudate nucleus and putamen. Partial demyelinization of globus pallidus. Anderson's modified Kulschitsky-Pal stain; ×2¾.

Fig. 8.—Left thalamus—coronal section. État marbré in medial nucleus. Modified Kulschitsky-Pal stain; ×3½.

Basal Ganglia.—A well-marked état marbré was present in the caudate nucleus and putamen of both sides of the brain (Fig. 7). . The myelinated networks were widely distributed throughout the ganglia, though densest in the lateral and dorsal part of the putamina. Except in the areas affected by hypermyelinization the large and small nerve cells were not noticeably reduced in numbers. The myelinated strands were the seat of a fibrillary gliosis and a finer proliferation of glial fibres was also visible in intermediate areas. No sign of regenerative activity was seen in the axis cylinders.

The globus pallidus of both sides showed glial sclerosis and poverty of myelinated fibres in its central portion (Fig. 7). There was marked beading of the remaining fibres in the areas poor in myelin.

The thalami were the seat of état marbré of a less pronounced character than that found in the striate bodies. It affected the medial nuclei (Fig. 8). Increase in glial fibres was present over a wide area and a close correspondence between gliosis and

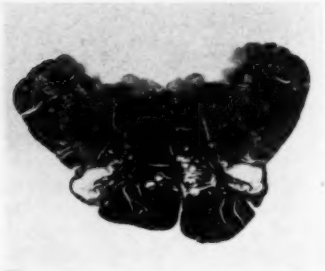

Fig. 9.—Atrophy of inferior olives. Kulschitsky-Pal stain; ×2½.

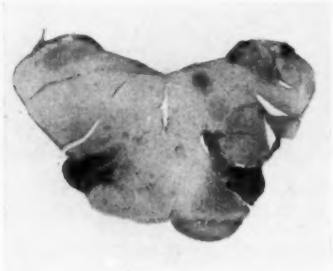

Fig. 10.—Sclerosis of inferior olives. Holzer stain; ×2½.

hypermyelinization could not be demonstrated. Except in the areas affected by état marbré there was no obvious nerve cell reduction.

The hypothalamic nuclei appeared normal.

Substantia nigra.—No cell loss or depigmentation was found in sections taken from several levels. The cephalad extremity of the substantia nigra showed some glial sclerosis without obvious changes in the nerve cells.

Pons.—Nerve cells and myelin preparations showed no abnormality. The Holzer stain revealed a well-marked proliferation of glial fibres in the transverse fibres and in the nuclei pontis. The pyramidal tracts did not share in this change.

Medulla.—Atrophy of the inferior olives was a conspicuous feature, the total size of these structures being greatly reduced. There was almost complete disappearance of nerve cells in the lateral portions, a few shrunken cells remaining in the ventral and medial coils. A gross reduction in numbers of myelinated fibres (Fig. 9) and an extremely dense glial sclerosis (Fig. 10) were present in the atrophic areas. Sections taken at different levels showed that both olives were affected in this way throughout the greater part of their extent. There was, however, little cell loss in the most cephalad portion, though here also an increase in glial fibres was present. The pyramidal tracts were normal.

Spinal Cord.—The cervical region of the spinal cord showed no pathological change as regards myelin or glia.

Discussion

One of the most remarkable features of this case is the discrepancy between the clinical condition (one common to a host of low-grade mental defectives)

and the gross and widespread lesions in the nervous system. There is, it is true, often little parallelism between the extent of cerebellar disease and the functional disability thereby produced. Time of onset seems to be an important factor in the production of symptoms, for some congenital cerebellar defects may have no obvious clinical consequences, e.g. the Arnold-Chiari deformity (Aring, 1938) and the lesser degrees of simple hypoplasia. Although in the present case it is impossible to date with accuracy the inception of the pathological process, some of the cerebellar abnormalities present appear to have dated from early life and are possibly congenital. The exposure of the white matter along the margins of the lateral lobes owing to the small size of the cerebellar folia in this situation is more suggestive of inhibited development than the result of atrophy and shrinkage of a previously fully formed organ. Also the fact that the main part of this small cerebellum showed but little evidence of pathological change supports this view. Small cerebella, the size of which is out of proportion to the extent of the histological lesions found in them, have frequently been reported in cases of adult cerebellar ataxia, especially in the hereditary spino-cerebellar form (Wilson, 1940), and it is not clear in such cases as to what emphasis should be laid upon the factors of " hypoplasia " or " atrophy " in discussing their pathogenesis. In the present case it seems reasonable to suppose that a process of atrophy starting not later than infancy has inhibited the growth of the cerebellum. This hypothesis of an infantile onset of atrophy is supported by the coincident changes in the basal ganglia, for, as previously pointed out, état marbré of the striatum in the majority of cases manifests itself in very early life.

Even more remarkable than the absence of cerebellar symptoms is the lack of clinical signs pointing to involvement of the corpus striatum. Had this patient been a typical example of double choreo-athetosis few surely would have doubted that the anatomical substratum of his physical condition lay in the lesions of corpora striata and thalami. It is true that athetosis may not be shown by cases in which the cerebral cortex, in particular the motor area, is atrophied (Norman, 1938), but in this instance no pyramidal tract or cortical lesion was found.

Furthermore, " while the rigidity and exaggerated postural fixation of extra-pyramidal disease can be regarded as ' corresponding opposites ' (Jackson) of cerebellar hypotonia, the diminution of certain automatic activities, as failure of the arms to swing in walking, the static tremor which may appear during the maintenance of posture, the poverty of automatic movements, the slowness of motion and the difficulty in performing alternate movements are symptoms common to disease of both the extra-pyramidal system and the cerebellum and indicate a functional relationship between these two organs " (Holmes, 1939). One would have thought, therefore, that a combination of cerebellar and striatal disease as in this case would have produced an increase and not a " cancelling out " of some of the above clinical signs. Although finer tests of co-ordination cannot be satisfactorily carried out on non-co-operative idiots, it is apparent that the clinical condition of this patient did not accord with such theoretical suppositions.

This case throws no light upon the question of ætiology either of état marbré or of cerebellar atrophy. The family history gave no indication that a genetic factor might be held responsible and the probable early onset of the pathological process hardly suggests a pre-senile degeneration in the sense implied by Scherer in his examples of adult olivo-ponto-cerebellar atrophy. With regard to état marbré, Scholz's conclusion that it is the result of " partial tissue necrosis " advances the problem of pathogenesis very little further than Vogt's original conception of " pathoclisis." Birth injury does not appear to be a factor in the present case. The demyelinization of the globus pallidus has also been described in cases of état marbré by Onari (1925), Meyer and Cook 1936), and Gozzano (1934). One is left with the rather nebulous conception of an atrophic process of unknown ætiology starting in early life and affecting more or less selectively and symmetrically the basal ganglia and the neo-cerebellar system with its olivary component.

Summary

In the brain of a 33-year-old non-epileptic idiot bilateral état marbré of caudate nucleus, putamen, and, to a lesser extent, thalamus was found. There was demyelinization of the central part of each globus pallidus. The cerebellum was considerably reduced in size, especially in the lateral lobes, where an atrophy of Purkinje cells was present chiefly affecting the superior and inferior semilunar lobules. The inferior olives were grossly atrophied and demyelinized save in their most cephalad parts. The nuclei pontis and transverse fibres of the pons showed mild glial sclerosis only. The cerebral cortex showed no atrophic changes. It is suggested that the element of hypoplasia shown by the cerebellum was due to the onset of atrophy prior to the full development of the organ. A peculiar feature of the case was the absence of clinical signs referable either to cerebellar or striate disorder.

References

Aring, C. D. (1938). *J. Neurol. Psychiat.* (New Series), **1,** 100.
Gozzano, M. (1934). *Riv. neurol.*, **7,** 1.
Guillain, G., Matthieu, P., and Bertrand, I. (1926). *Ann. Méd.*, **20,** 417.
Holmes, G. (1939). *Brain*, **62,** 1.
Meyer, A., and Cook, L. C. (1936). *J. Neurol. Psychopath.*, **16,** 341.
Norman, R. M. (1938). *J. Neurol. Psychiat.* (New Series), **1,** 7.
Onari, K. (1925). *Z. ges. Neurol. Psychiat.*, **98,** 457.
Scherer, H. J. (1933). *Ibid.*, **145,** 406.
Scholz, W., Wake, J., and Peters, G. (1938). *Ibid.*, **163,** 193.
Van Bogaert, L., and Bertrand, I. (1930). *Rev. Neurol.*, **2,** 617.
Wilson, S. A. K. (1940). *Neurology*. Arnold: London.

THE NEUROHISTOLOGICAL BASIS FOR THE SENSATION OF PAIN PROVOKED FROM DEEP FASCIA, TENDON, AND PERIOSTEUM

BY

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THE work of Waterston (1933*a*, *b*), Lewis (1938), Kellgren (1938), and others, as well as clinical experience, has established that pain can be aroused from deep fascia, tendon, and periosteum. The present paper deals with the neurohistological basis for the sensation of pain which can be aroused from these tissues.

Physiological Observations

Experiments were carried out on two human subjects. Sensations were aroused by means of fine, sharp needles.

Experiments on Deep Fascia and Tendon

Series 1.—Areas of skin and superficial fascia covering the junctions of the biceps brachii muscle with its tendon of insertion, and of the gastrocnemius and soleus muscles with the tendo Achillis, were anæsthetized by infiltration with 4 per cent. novocain solution containing 1 part in 20,000 adrenalin hydrochloride. Fine, sharp needles were inserted through the anæsthetized skin and superficial fascia. No sensations were recorded until the point of the needle reached the deep fascia or peritendinous connective tissue. At this level, either no sensation whatever or sensations of pressure or pain were recorded. Several varieties of pain were distinguished, all apparently commenced as soon as the stimulus was applied. Two main varieties were recorded. One was mild, gave the impression of being sharply " localized," disappeared as soon as the stimulus was removed, and was described as a prick. The other was more severe and diffuse in character, rose gradually in intensity to a maximum, then slowly receded and persisted for a short time after removal of the stimulus. It was described as an ache of peculiarly unpleasant quality. All varieties of pain were spatially independent, the second main variety being experienced more commonly when thicker needles were used.

Series 2.—The skin and superficial fascia over the same musculo-tendinous junctions were anæsthetized as before, and, in addition, the novocain and adrenalin solution was injected into the deep fascia and over the surface of the connective tissue investment of the tendon. Experiments were carried out

fifteen to twenty-five minutes later. No sensations were aroused until the needle was introduced into the substance of the tendon, when pain was provoked but rarely, and was constantly of the first variety described. Pain of the second variety could not be aroused even when a relatively thick needle, such as a No. 17 hypodermic, was used. On one occasion a single contraction of an isolated group of fibres of the gastrocnemius muscle was observed on insertion of the needle into the tendon substance; this was unaccompanied by any sensation whatever. Pain was aroused when the needle was reinserted into approximately the same site, but no further muscular contraction was observed.

Series 3.—Areas of skin and superficial fascia over the tendo Achillis at a distance of about 7 cm. from the musculo-tendinous junction were anæsthetized. From the deep fascia and peritendinous connective tissue pressure and pain were aroused, as in the first series of experiments. No pain could be aroused from the substance of the tendon in this position before or after anæsthetization of its connective tissue sheath and the overlying deep fascia. A feeling of tension could only be provoked when the tendon was moved as a whole for distances of at least $\frac{1}{4}$ cm. This sensation was not " localized," but gave the impression of a mass movement of the whole tendon.

Experiments on Periosteum

Areas of skin and superficial fascia over the subcutaneous surface of the tibia were anæsthetized. Fine, sharp needles were inserted through the anæsthetized areas as far as the bone. Several varieties of pain were aroused from periosteum; they were similar to those provoked from deep fascia and tendon connective tissue sheath, except that the first main type of pain described was frequently referred to a point 2 or 3 cm. distal to the site of application of the stimulus. No other sensations were provoked from the subcutaneous surface of the tibia.

The number of spots from which pain could be aroused in periosteum, deep fascia, and peritendinous connective tissue was less than in the skin of the same subjects (Woollard, Weddell, and Harpman, 1940).

Histological Observations

Deep Fascia.—In methylene blue preparations of deep fascia from the human leg, three types of nerve ending were found. Finer medullated and non-medullated nerve fibres form a loose-meshed plexus and give rise to free nerve terminals (Fig. 1). Vater-Pacini and Golgi-Mazzoni corpuscles also occur (Figs. 2 and 3). Many of the Vater-Pacini corpuscles receive, in addition to the principal thick medullated fibre, a fine non-medullated " accessory " nerve fibre which terminates by forming a coil with and around the principal nervous component of the ending (Fig. 2).

Tendon.—In methylene blue preparations of tendons from the extensor muscles of the leg of the rabbit, neuro-tendinous endings of Golgi were found in the vicinity of the musculo-tendinous junction (Figs. 4 and 5). These endings may be disposed in groups (Fig. 4) or as units (Fig. 5). In every instance the specialized ending is borne by a single, thick nerve fibre which is usually

Fig. 1.—Photomicrograph showing a plexus of finer medullated and non-medullated nerve fibres giving rise to free nerve endings; deep fascia of the human leg. Methylene blue preparation. ×520.

Fig. 2.—Photomicrograph showing a Vater-Pacini corpuscle in the deep fascia of the human leg. The arrow points to the " accessory " fibre. Methylene blue preparation. ×475.

Fig. 3.—Photomicrograph showing Golgi-Mazzoni corpuscles in the deep fascia of the human leg. Methylene blue preparation. ×600.

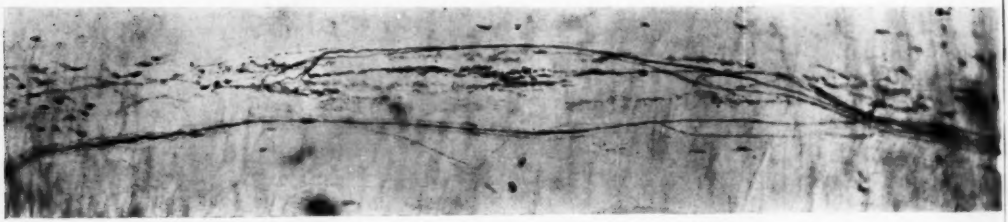

Fig. 4.—Photomicrograph showing a group of neuro-tendinous endings of Golgi and free nerve endings derived from " accessory " fibres in the vicinity of the musculo-tendinous junction of the extensor digitorum longus muscle of the rabbit. Methylene blue preparation. ×220.

Fig. 6.—Photomicrograph showing free nerve endings derived from an " accessory " fibre accompanying the principal nerve fibre of a Golgi neuro-tendinous ending; the latter is seen in the background. Tendon of the tibialis anticus muscle. Methylene blue preparation. ×440.

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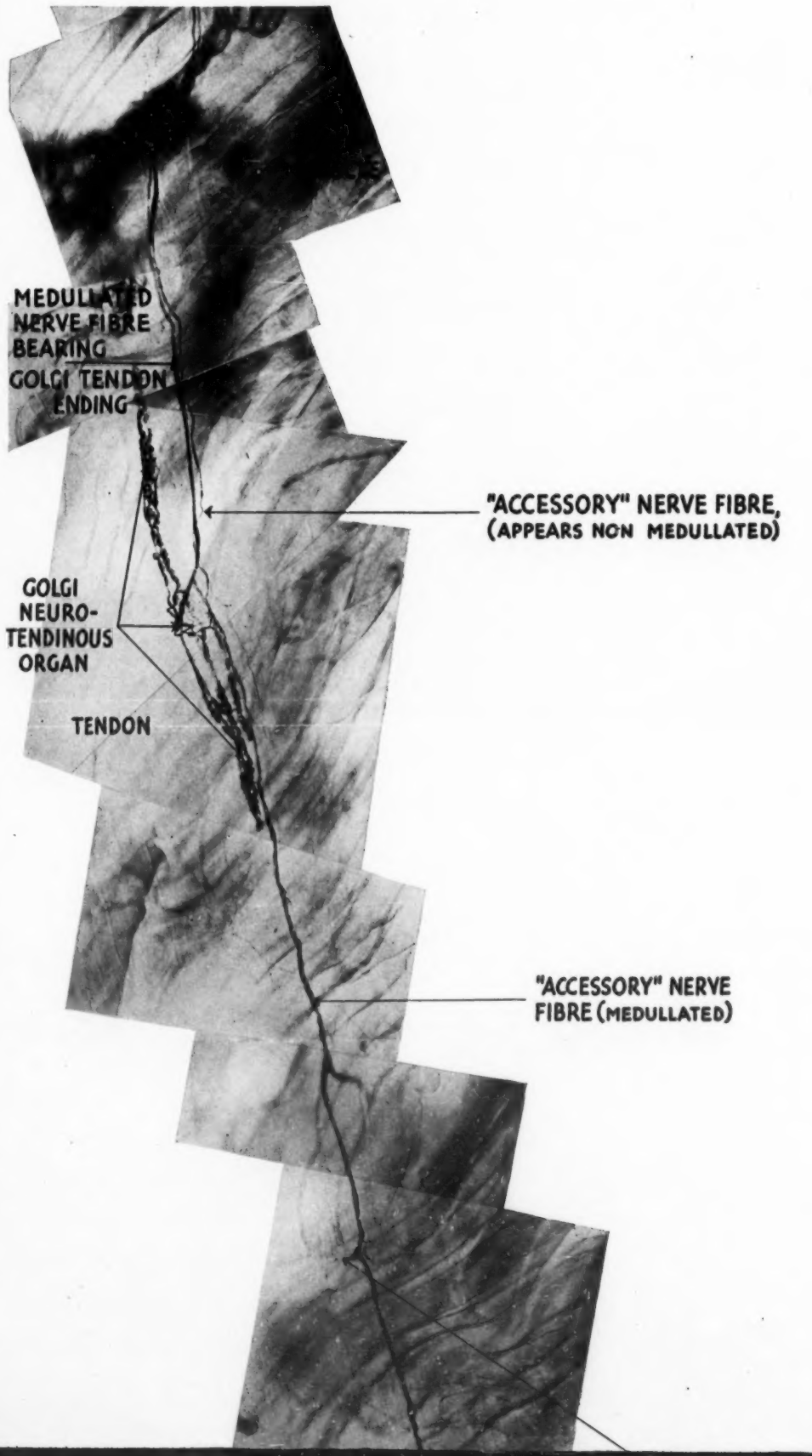
MEDULLATED NERVE FIBRE BEARING GOLGI TENDON ENDING
"ACCESSORY" NERVE FIBRE, (APPEARS NON MEDULLATED)
GOLGI NEURO-TENDINOUS ORGAN
TENDON
"ACCESSORY" NERVE FIBRE (MEDULLATED)

"ACCESSORY" NERVE
FIBRE (MEDULLATED)
FREE NERVE
ENDINGS

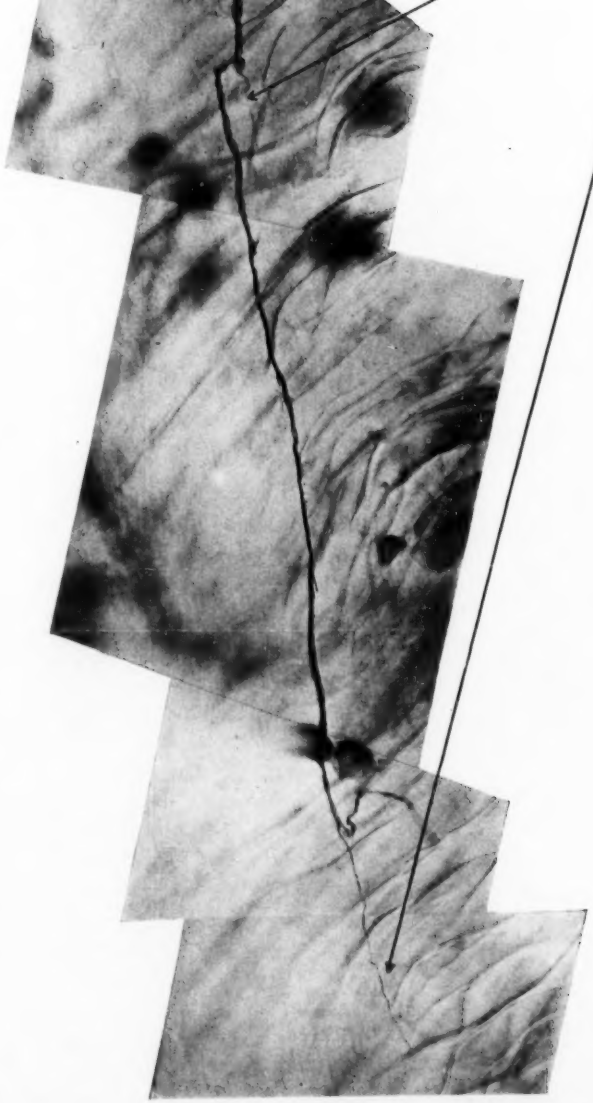

Fig. 5.—Photomicrograph showing a neuro-tendinous ending of Golgi and the " accessory " nerve fibre giving rise to free nerve endings at the musculo-tendinous junction. The relative fibre directions have become displaced during histological preparation. In the original preparation the medullated and non-medullated portions of the accessory nerve fibre were clearly seen to be in continuity. This is not obvious in the photomicrograph owing to the varying focal planes occupied by the nerve fibre. Methylene blue preparation, Rabbit ×300.

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medullated. This fibre is constantly accompanied by an " accessory " nerve fibre which, proximal to the ending, is thin and non-medullated. In the neighbourhood of the neuro-tendinous ending the " accessory " fibre gives rise to fine, varicose, free nerve terminals (Figs. 4, 5, and 6). The " accessory " fibre extends distal to the Golgi ending, becomes thicker in diameter, may become medullated (Fig. 5), and at intervals gives rise to further free nerve endings. The " accessory " fibre in question is similar to " accessory " nerve

Fig. 7.—Photomicrograph showing a Meissner corpuscle in the human thumb; the arrow indicates the " accessory " nerve fibre, which expands as it approaches the corpuscle and gives rise to free nerve endings. Reduced silver preparation. ×570.

fibres ending in close relation to encapsulated receptors elsewhere (Figs. 2 and 7).

Periosteum.—In methylene blue preparations of periosteum from the mandible of the rat there occur finer medullated and non-medullated nerve fibres giving rise to free nerve endings (Fig. 8). These fibres are arranged in a simple plexiform manner. Endings of tension recording type occurring in periosteum at the origin of the genioglossus muscle in the rat have been described elsewhere (Weddell, Harpman, Lambley and Young, 1940).

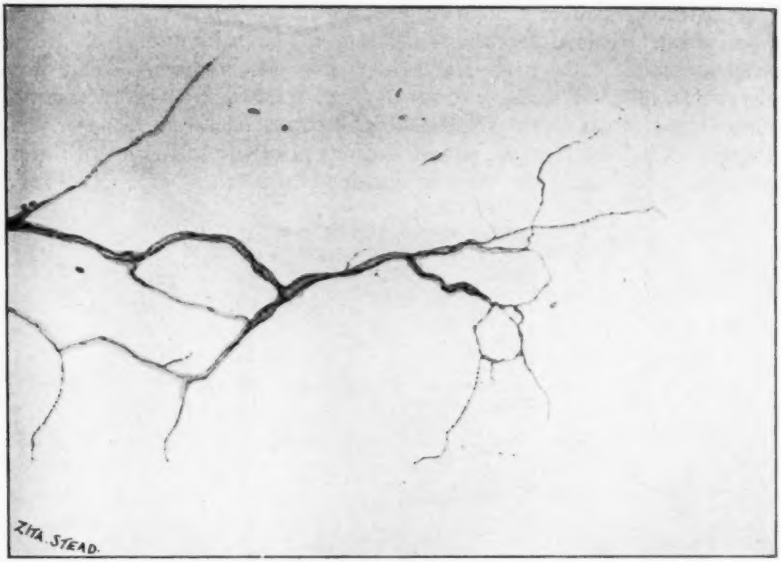

Fig. 8.—Drawing illustrating the plexus of nerve fibres giving rise to free nerve endings in the periosteum of the mandible of the rat. Methylene blue preparation. ×700.

In none of the plexuses mentioned was continuity between nerve fibres observed.

Discussion and Interpretation of Results

Woollard, Weddell, and Harpman (1940) have established that in human skin pain is subserved by the medullated and non-medullated nerve fibres bearing free nerve endings. Stimulation of morphologically similar fibres and endings in the skin of the ear of the rabbit evokes struggling. Similar somatic fibres and endings occur in teeth (Schafer, 1934; Maximow and Bloom, 1938; Lewinsky and Stewart, 1938*a*; Tiegs, 1932, 1938; and others), the cornea (Ranvier, 1878; Dogiel, 1890; Attias, 1912; Agababow, 1912; Kadanoff, 1928; Cajal, 1933; present authors; and others), tympanic membrane (Wilson, 1911), mucous membranes (Huber, 1900; Retzius, 1908; Kadanoff, 1927; Cajal, 1933; Lewinsky and Stewart, 1938*b*, 1939); Stewart and Lewinsky, 1939), serous membranes (Dogiel, 1902; Timofeew, 1902; Michailow, 1908; Boeke, 1932; and others), intermuscular connective tissue (Hinsey, 1927, 1930; Boeke, 1932), surface of tendons (Boeke, 1932), dura mater (Stoehr, 1932), and the adventitia of blood vessels (Woollard, 1926; Hinsey, 1927, 1928, 1930; Woollard *et al.*, 1940), from all of which pain can be aroused (Foerster, 1927; Capps and Coleman, 1932; Waterston, 1933*b*; Lewis, 1938; Kellgren, 1938; Lewis and Kellgren, 1939; and others). Only free nerve terminals occur in teeth, the central part of the cornea, and the tympanic membrane; from these structures pain only can be provoked (*v.* Frey, Strughold and Karbe, 1925;

Clark, 1939). The finding that after cocainization of the cornea conjunctiva a sensation of contact can be evoked from the cornea (Nagel, 1895; Marx, 1921; Pritchard, 1931) is explicable on the grounds of stimulation of extra-corneal sensory nerve endings by deformation, an interpretation suggested by the findings of Carmichael and Woollard (1933). It may be concluded that pain is subserved by free nerve endings. The anatomical work of Ranson (1913, 1914, 1931), the physiological observations of Ranson and Billingsley (1916), the cathode-ray oscilloscope studies of Gasser and Erlanger (1939), Gasser (1935), Heinbecker, Bishop and O'Leary (1934) and Clark, Hughes and Gasser (1935), and the histological and physiological observations of Woollard *et al.* (1940) concur in showing that pain is transmitted by finer medullated and non-medullated fibres. The specificity of the nerve fibres and endings subserving pain has been established by the work of Adrian (1926, 1932), Cattell and Hoagland (1931), Heinbecker and Bishop (1935), and Woollard *et al.* (1940). Woollard *et al.* (1940) have reviewed the literature in detail, and criticize on grounds of technique an observation by Heinbecker *et al.* (1934) that throws doubt upon the strict specificity of the fibre group conducting pain impulses.

The physiological and histological observations recorded in the present paper and the facts to which brief reference has been made above lead to the conclusion that in deep fascia, periosteum, peritendinous connective tissue, and tendon substance pain is subserved by free nerve terminals borne by finer medullated and non-medullated nerve fibres. The sensations of pressure aroused in the first and third series of experiments are explained by the occurrence of Vater-Pacini and Golgi-Mazzoni corpuscles in deep fascia; that such a function is subserved by these endings is generally accepted. With regard to tendon substances, the observations here recorded show that in man, subject to the conditions of the experiments performed, pain can only be aroused from tendon substance, as opposed to its immediate coverings, at relatively few points near the musculo-tendinous junction. In the rabbit this is the only region in which nerve fibres and endings can be demonstrated in tendon. The endings are of two types: the first is the neuro-tendinous ending of Golgi, to which is attributed the function of recording tension (Matthews, 1933); the second type is similar to the " accessory " innervation to encapsulated endings subserving touch, cold, and pressure described by Timofeew (1895), Ruffini (1902), Dogiel (1892, 1893, 1904), Sokolow (1899), Sala (1899), Sfameni (1901), Michailow (1908), Ohmori (1923), Jalowy (1935), Woollard (1936, 1937), Woollard *et al.* (1940) and others. Lavrenko (1938) has shown that this " accessory " innervation is somatic. Woollard (1937) and Woollard *et al.* (1940) have remarked upon the morphological similarity between " accessory " nerve fibres and endings and the nerve fibres and endings that subserve pain in the human skin; Woollard (1937) has described an " accessory " fibre and ending, derived from the sub-epidermal plexus that subserves pain, to a Krause end bulb. It is presumed that in man pain aroused from tendon is subserved by a terminal nerve apparatus similar to the " accessory " innervation to Golgi tendon endings in the rabbit. Woollard (1936) has suggested that the function of such an " accessory " innervation is to protect the " principal " receptor from damage.

Goldscheider's (1926) conception that excessive stimulation of nerve-endings recording deformation results in pain may be explained by the above findings.

That the " accessory " fibre to the Golgi tendon ending probably acquires a medullary sheath where it increases in diameter is explicable by Duncan's (1934) theory of progressive myelinization with increasing diameter of nerve fibres. The physiological significance of such changes in diameter is doubtful.

Rosenbach (1884), Gad and Goldscheider (1892, 1898), Thunberg (1902), Alrutz (1909), and Lewis and Pochin (1937), have shown that from human skin two types of pain can be aroused. Woollard *et al.* (1940) consider that there are all gradations between two main varieties of cutaneous pain, which they describe as follows: " . . . the first being abrupt in onset, hurting little, and lasting for a period corresponding to that during which the stimulus (a fine, sharp needle) is being applied; the second is delayed in onset, rises gradually in intensity, gives the impression of a small stinging area, and disappears slowly." Lewis and Pochin (1937) and Woollard *et al.* (1940) have recently discussed the various anatomical and physiological explanations which have been advanced to account for this multiplicity of types of cutaneous pain. Woollard *et al.* (1940) have presented evidence suggesting that the first main type of cutaneous pain is due to stimulation of units of the cutaneous nerve apparatus subserving pain, whilst the second main variety is due to stimulation of bundles of the nerve plexus in question. From the substance of tendon in man pain of only one variety, corresponding to the first type of cutaneous pain, can be aroused. In the substance of tendon in the rabbit only units of the terminal nerve apparatus presumed to subserve pain can be demonstrated. From deep fascia, peritendinous connective tissue, and periosteum pain similar to the first as well as pain resembling the second main variety of cutaneous pain can be aroused, the latter being more often provoked by relatively thick as opposed to fine needles. The second main variety of pain differs from its cutaneous counterpart in that there is no delay in its onset, it is more severe, and described as disagreeable rather than stinging. Histologically, deep fascia and periosteum are supplied by both single nerve fibres and bundles of nerve fibres bearing free nerve endings. The bundles, however, contain relatively fewer fibres than they do in the cutaneous plexuses that subserve pain in human and, by inference, rabbit skin. The present findings thus lend support to the conclusion that the varieties of pain which can be aroused from definitive organs are determined by the morphological disposition of the terminal nerve fibres subserving pain, and not by a multiplicity of afferent dorsal root systems as concluded by Lewis and Pochin (1937, 1938); further aspects of the theory propounded by these authors have been discussed elsewhere (Woollard *et al.*, 1940). Heinbecker and Bishop (1935) have recorded observations which they interpret as suggesting that electrical stimulation of pain receptors is essentially nerve fibre stimulation.

Kellgren (1938) states that the introduction of a hypodermic needle through anæsthetized skin into tendon occasionally arouses a " purely local " pain, whilst the injection of 0·05 c.c. of 6 per cent. aqueous sodium chloride solution into the substance of tendon provokes " diffuse " pain felt over a small area

somewhat distal to the point of injection. The author also states that a sharply localized as well as a diffuse type of pain can be aroused on injection of small quantities of sodium chloride solution into various muscles. Lewis (1938) states that on introduction of a needle through locally anæsthetized skin " each time the needle is jabbed against the tibia a disagreeable diffuse pain is produced, which lasts, at its height, for an appreciable time," and that pain provoked from periosteum is " located with much accuracy." Kellgren (1938) remarks that scratching of the fascial sheath covering the tendon of the tibialis anticus muscle by a needle introduced through locally anæsthetized skin provoked pain " which was always recognized as coming from a point localized regularly about 2 cm. distal to the needle by most subjects and accurately at the needle by a few," In the present experiments pain aroused from tendon, peritendinous connective tissue and periosteum was generally accurately localized. Sometimes, however, pain aroused from periosteum was believed by the subject to be evoked from a point about 1 in. distal to the point of stimulation. The anatomical basis for this fact has not been determined.

Conclusions

Pain of two main varieties can be aroused from deep fascia, peritendinous connective tissue, and periosteum. The first is similar to the first main type of cutaneous pain described by Woollard *et al.* (1940); the second main variety corresponds to the second main type of cutaneous pain, but is different in quality and time relation to the stimulus.

From tendon substance pain can only be aroused near musculo-tendinous junctions; it is of only one variety, corresponding to the first main type of cutaneous pain.

The experiments and observations recorded suggest that there is an " accessory " innervation to neuro-tendinous endings of Golgi in man, and that stimulation of the " accessory " fibre or ending gives rise to pain.

There is a similar " accessory " innervation to encapsulated receptors recording touch, pressure, and cold.

The present findings lend support to a previous conclusion that the varieties of pain which can be aroused from definitive organs are determined by the morphological disposition at the periphery of the nerve fibres and endings subserving pain.

References

Adrian, E. D. (1926). *J. Physiol.*, **62**, 33.
—— (1932). *The Mechanism of Nervous Action.* Philadelphia.
Agababow, G. (1912). *Arch. Ophthal.*, **83**, 317.
Alrutz, S. (1909). *Skand. Arch. Physiol.*, **21**, 237.
Attias, G. (1912). *Arch. Ophthal.*, **83**, 207.
Boeke, J. (1932). *Cytology and Cellular Pathology of the Nervous System.* Ed. by W. Penfield. New York, **1**, 241.
Cajal, S. Ry. (1933). *Histology*, London.
Capps, J. A., and Coleman, G. H. (1932). *An Experimental and Clinical Study of Pain in the Pleura, Pericardium, and Peritoneum.* New York.
Carmichael, E. A., and Woollard, H. H. (1933). *Brain*, **56**, 109.
Cattell, McK., and Hoagland, H. (1931). *J. Physiol.*, **72**, 392.
Clark, D., Hughes, J., and Gasser, H. S. (1935). *Amer. J. Physiol.*, **114**, 69.
Clark, W. E. Le Gros (1939). *The Tissues of the Body.* Oxford University Press.

Dogiel, A. S. (1890). *Anat. Anz.*, **5**, 483.
—— (1892). *Int. Schr. Anat. Physiol.*, **9**, 76.
—— (1893). *Arch. mikr. Anat.*, **41**, 585.
—— (1902). *Ibid.*, **59**, 1.
—— (1904). *Anat. Anz.*, **25**, 558.
Duncan, D. (1934). *J. comp. Neur.*, **60**, 437.
Foerster, O. (1927). *Die Leitungsbahnen des Schmerzgefuehls und die chirurgische Behandlung die Schmerzzustande.* Berlin and Vienna.
Gad and Goldscheider, A. (1892, 1898). Quoted by T. Lewis and E. E. Pochin (1937). *Clin. Sci.*, **3**, 1.
Gasser, H. S. (1935). *Proc. Ass. Res. nerv. ment. Dis.*, **15**, 35.
Gasser, H. S., and Erlanger, J. (1929). *Amer. J. Physiol.*, **88**, 581.
Goldscheider, A. (1926). *Handb. norm. path. Physiol.* Ed. by A. Bethe. Berlin, **11**, 131.
Heinbecker, P., and Bishop, G. H. (1935). *Proc. Ass. res. nerv. ment. Dis.*, **15**, 226.
Heinbecker, P., Bishop, G. H., and O'Leary, J. (1934). *Arch. Neurol. Psychiat., Chicago*, **31**, 34.
Hinsey, J. C. (1927). *J. comp. Neurol.*, **44**, 87.
—— (1928). *Ibid.*, **47**, 23.
—— (1930). *Proc. Ass. Res. nerv. ment. Dis.*, **9**, 153.
Huber, G. C. (1900). *J. comp. Neurol.*, **10**, 135.
Jalowy, B. (1935). *Z. Zellforsch.*, **23**, 85.
Kadanoff, D. (1927). *Z. Zellforsch.*, **5**, 615.
—— (1928). *Ibid.*, **7**, 553.
Kellgren, J. H. (1938). *Clin. Sci.*, **3**, 175.
Lavrenko, V. V. (1938). *Bull. Biol. et de med. exp.*, **5**,
Lewinsky, W., and Stewart, D. (1938*a*). *Brit. dent. J.*, **65**, 687.
—— (1938*b*). *J. Anat.*, **72**, 531.
—— (1939). *Ibid.*, **74**, 53.
Lewis, T. (1938). *Brit. med. J.*, **1**, 321.
Lewis, T., and Kellgren, J. H. (1939). *Clin. Sci.*, **4**, 47.
Lewis, T., and Pochin, E. E. (1937). *Ibid.*, **3**, 67.
—— (1938). *Ibid.*, **3**, 141.
Marx, E. (1921). *Extrait des annales d'occulistique*, 158.
Matthews, B. H. C. (1933). *J. Physiol.*, **78**, 1.
Maximow, A. A., and Bloom, W. (1938). *Textbook of Histology*, 3rd ed., Saunders, Philadelphia and London, 373.
Michailow, S. (1908). *Arch. mikr. Anat.*, **71**, 254.
Nagel, W. A. (1895). *Pflueger's Arch.*, **59**, 563.
Ohmori, D. (1923). *Z. Anat. Entw.*, **70**, 346.
Pritchard, E. A. B. (1931). *Brain*, **54**, 350.
Ranson, S. W. (1913). *J. comp. Neurol.*, **23**, 259.
—— (1914). *Ibid.*, **24**, 531.
—— (1931). *Arch. Neurol. Psychiat., Chicago*, **26**, 1122.
Ranson, S. W., and Billingsley, P. R. (1916). *Amer. J. Physiol.*, **40**, 571.
Ranvier, M. L. (1878). *Leçons sur l'histologie du système nerveux.*, Paris, 2 vols.
Retzius, G. (1908). *Proc. roy. Soc., B*, **80**, 414.
Rosenbach (1884). Quoted by T. Lewis and E. E. Pochin (1937). *Clin. Sci.*, **3**, 1.
Ruffini, A. (1902). *Bibliogra. anat.*, **11**, 267.
Sala, G. (1899). *Anat. Anz.*, **16**, 193.
Schafer, E. A. Sharpey- (1934). *Essentials of Histology*, 13th ed., 333.
Sfameni, P. (1901). *Arch. ital. Biol.*, **35**, 198.
Sokolow, A. (1899). *Anat. Anz.*, **16**, 452.
Stoehr, Ph., Jr. (1932). *Cytology and Cellular Pathology of the Nervous System.* Ed. by W. Penfield. New York, **1**, 381.
Stewart, D., and Lewinsky, W. (1939). *Proc. roy. Soc. Med.*, **32**, 1054.
Strughold, H., and Karbe, M. (1925). *Z. Biol.*, **83**, 189, 201, 207, 297.
Thunberg, T. (1902). *Skand. Arch. Physiol.*, **12**, 394.
Tiegs, O. W. (1932). *J. Anat.*, **66**, 622.
—— (1938). *Ibid.*, **72**, 234.
Timofeew, T. (1895). *Anat. Anz.*, **11**, 44.
—— (1902). *Arch. mikr. Anat.*, **59**, 629.
Waterston, D. (1933*a*). *J. Physiol.*, **77**, 251.
—— (1933*b*). *Lancet*, 943.
Weddell, G., Harpman, J. A., Lambley, D. G., and Young, L. (1940). *J. Anat.*, **74**, 255.
Wilson, J. G. (1911). *Amer. J. Anat.*, **11**, 101.
Woollard, H. H. (1926). *Heart*, **13**, 319.
—— (1936). *Brit. Med. J.*, **2**, 861.
—— (1937). *J. Anat.*, **71**, 480.
Woollard, the late H. H., Weddell, G., and Harpman, J. A. (1940). *Ibid.*, **74**, 413.

JUVENILE PARESIS IN ONE TWIN

BY

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(RECEIVED 24TH JULY, 1940)

Introduction

IT is now widely accepted that congenital syphilis is an infection that is acquired *in utero* from the mother, usually in the later months of pregnancy. It is not perhaps so widely recognized that in the case of twin pregnancies it is not unusual for the twins to suffer the luetic infection unequally. One twin may be born healthy, the other diseased; or if both are diseased the symptoms may appear at differing periods after birth and vary in severity in the two infants. This may be true for monozygous as well as dizygous twins. A considerable number of cases illustrating these facts have now been published, and the reader may be referred to the papers with bibliographies of Haslund (1924) and Bergel and Zimmermann (1932).

" The literature of syphilis," said Jonathan Hutchinson, " is encumbered with ill-founded opinions and untrustworthy facts." It is unfortunate that in many of the cases reported in the era of the Wassermann reaction, the " healthy " twin has been kept under observation for a few weeks or months only. The syphilitic twin has usually died and a post-mortem has established the diagnosis. The zealous author, fearful lest his enthusiasm should wane, records the case without observation of the apparently unaffected twin over a sufficiently lengthy period of time to prove the freedom from latent infection. In rare cases the twins survive infancy, and symptoms of delayed congenital syphilis appear in later childhood. Here again it is not infrequent to find total escape or mild infection of one twin while the other shows the disease in severe degree.

The following exposition of a case of juvenile paresis in one twin, the other twin completely escaping infection, provides further proof of the vagaries of prenatal infection. The twins have been under observation at the West London Hospital for the past seven years. Repeated clinical examinations and serological tests of blood and cerebrospinal fluid have been made over this period, not only on the twins but on the other members of the family.

Case Records

George and Thomas R., aged 17 years, are twin brothers of a second pregnancy. There is one older brother, James R., aged 27 years. The mother has been pregnant

on two occasions only, and there have been no miscarriages. Her health during pregnancy was excellent and the twin labour was normal. George, the smaller twin, who weighed 5½ lb. at birth, was born one hour before Thomas, who weighed 6¾ lb. at birth. Both twins were breast fed for 9 months.

The Affected Twin.—George R. at birth was smaller than his twin brother and was always more backward physically and mentally. During infancy he suffered from chicken-pox and measles, but never had a sore, and never suffered from rash, sore mouth, eye trouble, or convulsions. At the age of 5 years he went to school, but could not learn as well as his twin. When 10 years of age his physical condition began to deteriorate and he was sent for some months to Harefield Sanatorium under suspicion of tuberculosis. The diagnosis of tuberculosis was never confirmed, but it was found at the Sanatorium that his blood Wassermann was positive. Between the ages of 11 and 15 years he was treated as an out-patient at the West London Hospital Clinic, receiving in all 10 gm. of N.A.B. and 60 c.c. of bismuth compounds. At the age of 15 years the blood Wassermann was strongly positive and the blood Kahn was weakly positive. The cerebrospinal fluid was not examined. He then ceased to attend.

At the age of 17 years he was brought by his mother to the West London Hospital Neurological Department. She stated that he had left school at the age of 14 years 9 months, but had never been able to go to work. Although he had passed through a Board School education and had learned to spell, write, and perform simple calculations, and could at that time be trusted with money, he was regarded by his mother as a backward child. His disposition had been affectionate and quiet. From the age of 15 years mental deterioration had set in, thought by the parents to be due to a slight head injury. He became more childish in every way. If told to wash he would put his hands in the water but not rinse or soap them, he lost the ability to dress himself, and would not clean his shoes. Bursts of irritability were frequent, when he would pinch or kick his parents or throw knives, forks, or plates at those with whom he was annoyed. He became very sensitive to noise and would display temper if something was said to him which he could not understand. His memory failed, so that he could no longer be trusted to perform errands or be trusted with money. He retained, however, the names of the football teams which he continued to mark on his weekly coupon. If left alone in the house he would mischievously switch on lights and wireless, open the windows, and carelessly let the fire go out. In attempting to relight the fire he would strew ashes and wood and paper on the carpet. He could no longer read, write, or calculate. His speech became stuttering, rapid, and indistinct. No fits or convulsions had occurred.

On examination at the age of 17 years the patient weighed 87½ lb. and his height was 62½ inches. Stigmata of congenital syphilis were absent. Specifically he showed no Hutchinson's teeth, no interstitial keratitis or chorio-retinitis, no rhagades, deafness, nor sabre deformities of the tibiæ. He was of poor nutrition and physique, and exceedingly tremulous, ataxic, and dysarthric. His speech was indistinct, precipitate, and toneless. He stuttered and repeated the end syllables of words. His stutter was accompanied by overaction and tremors of the facial muscles and lips, and a constant tic-like protrusion of the tongue. Vocabulary was limited and he had difficulty in forming sentences. He could recognize and name objects and well-known persons portrayed in a picture paper. The optic discs, pupils, and cranial nerves were all normal apart from coarse tremors of the lips and tongue. The upper limb movements were clumsy and inco-ordinate, and the gait was wide-based, reeling, and ataxic so that he needed support to walk. This ataxia was of the cerebellar type. The biceps, triceps, and supinator jerks were all brisk and equal. Both plantar responses were extensor ; the abdominal reflexes were present upper and lower. Sensory testing in detail was not possible owing to his mental state, but vibration and sense of position appeared normal, and there was no defect of pain on pressure of the Achilles tendons. The heart was normal in size and the sounds clear. The resting pulse rate was 70 per minute, the blood pressure = 120/65. No disease could be detected in the chest or

abdomen. The urine was acid and had a sp. gr. 1,020 and contained no albumen or sugar.

He was removed at the request of his mother to Springfield Mental Hospital. There he lay restlessly in bed, playing untidily with a child's pack of cards. Malarial treatment had been given, with little effect on the mental condition.

The cerebrospinal fluid analysis on admission showed: Cells=25 per cu. mm. (50 per cent. small mononuclear; 40 per cent. medium mononuclear; 10 per cent. large mononuclear); globulin=Pandy+++, Nonne Apelt+++; albumen=0·1 per cent.; chlorides=730 mgs. per cent.; Lange curve=5.5.5.5.5.5.5.4.3.2; Kahn=strong positive; W.R.=positive++; blood Kahn=positive 2·1; blood W.R.=strong positive++.

The Healthy Twin.—Thomas R. was physically and mentally normal from birth. He went to school aged 5 years and left at the age of 14 years to work in a celluloid factory. The blood Wassermann reaction and Kahn tests were negative when he was aged 11, and between the ages of 11 and 14 years four similar tests at intervals gave negative results. He now works as a machine hand in a factory.

Examination at the age of 17 years showed that he was a mentally alert young man of good nutrition and physique. His weight was 134 lb. and his height 70½ inches. Stigmata of congenital syphilis were absent. His speech and articulation were normal and no tremors of the tongue, face, or limbs were observed. The optic discs, pupils, and cranial nerves were normal. The limbs were strong and steady at all joints, and there was no ataxia on walking. Detailed sensory testing revealed no abnormality. The tendon reflexes were brisk and equal, the plantar responses flexor, and the abdominals brisk, upper and lower. The heart was normal in size and the sounds clear. The resting pulse rate was 65 per minute and the blood pressure measured 130/65. There was no disease in the chest or abdomen and the urine was normal.

The cerebrospinal fluid analysis at the age of 17 years showed: Cells=0 per cu. mm.; total protein=0·025 per cent.; globulin=Pandy—a faint trace, Nonne Apelt—a faint trace; Lange curve=1.1.0.0.0.0.0.0.0.0.; Kahn=negative; W.R. =negative. Blood Wassermann and Kahn tests (the fifth time of testing) were completely negative.

The Sib.—The elder brother, James R., aged 27 years, is a builder. He showed no clinical abnormality on detailed testing, and the blood Wassermann reaction was negative. He is married and has two healthy children.

The Father.—The father, William R., aged 46 years, is a fitter. He has always been healthy except for a recent duodenal ulcer, and he denies venereal disease. Detailed neurological and general physical examinations reveal no abnormality. The blood Wassermann and Kahn tests were negative at the age of 46 years.

The Mother.—The mother, Mrs. Eleanor R., is aged 46 years. The twins were born in 1922, when she was 29 years old, four years after her husband's return from active service in France and Italy, 1914 to 1918. At the age of 38 years she attended the West London Hospital for what at first appeared to be a suppurating pre-patellar bursa of the left knee which was soon found to be a gumma. The blood W.R. was then ++++ and the Kahn test positive 4.4.3. After treatment for four years the blood W.R. was ++ and the Kahn 2.2.

On examination at the age of 46 years she showed no clinical abnormality on detailed testing other than a healed scar on the front of the left knee. The blood Wassermann was still ++ and the Kahn test positive.

The cerebrospinal fluid analysis showed: Cells=2 per cu. mm.; total protein =0·01 per cent.; Lange curve=0.0.0.0.0.0.0.0.0.0.; W.R.=completely negative.

Data Regarding the Twinning

There is a marked family history of twinning on the mother's side of the family. Her mother, Mrs. B., had a twin miscarriage (4½ months), and Mrs. B.'s sister had

twin boys. Mrs. R.'s maternal grandmother had twins, a boy and a girl. The wife of Mrs. R.'s brother, Alfred, has twin sons.

Thomas and George R. are dizygous twins. I am indebted to Dr. R. Race, of the Galton Laboratory Serum Unit, University College, London, for proving this conclusively for me. In Dr. Race's investigations the M N blood-group system settled the zygosity. Thomas was O N and George O M N (Fig. 1).

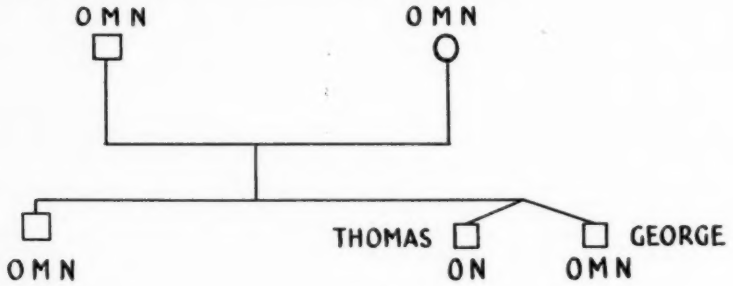

Fig. 1.

There is no connection between the A B O system and the M N. They are inherited on different pairs of chromosomes.

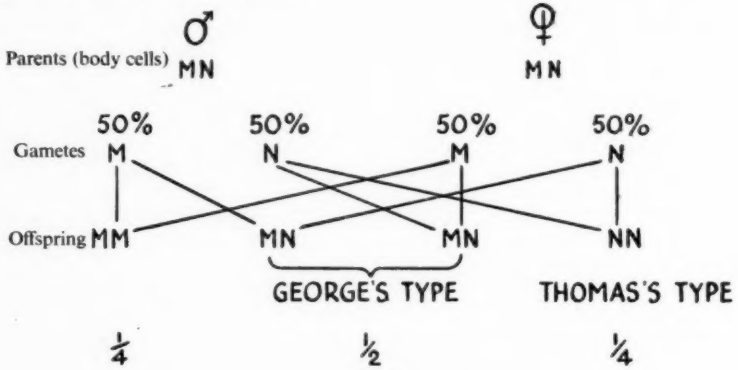

Fig. 2.

George has had an M from one parent and an N from another, while Thomas has had an N from both (N N or M M are called N or M) (Fig. 2).

Anthropometric observations regarding iris colour and pigment pattern, hair colour and whorl, fingerprints, etc., corroborated that the twins were dissimilar.

Discussion

Even in the absence of stigmata of congenital syphilis it seems unlikely that the infection of the paretic twin was a post-natally acquired one. According to Menninger congenital syphilitic stigmata are completely absent in 25 per cent. of juvenile paretics. No history of primary sore or rash in George's childhood could be ascertained. As in most cases of congenital syphilis the mother showed signs of the infection but not the father.

Mental retardation had been present since infancy. Physical deterioration began at the age of 10 years, but it was not until five years later that mental deterioration and regression commenced. It is likely that the early mental retardation was due to congenital syphilis. Approximately 40 per cent. of all cases of juvenile paresis are feeble-minded from birth, although the disease classically begins in a previously normal child in later childhood. Not all cases of feeble-mindedness due to syphilis turn out to be cases of juvenile paresis, nor will the finding of a paretic gold curve alone in the spinal fluid justify the diagnosis of paresis. The clinical examination must demonstrate the neurological signs of the disease and the serological picture in the spinal fluid must be complete in respect of pleocytosis, increase in globulin, and positive Wassermann reaction. In the feeble-minded group of congenital paretics the disease is insidious in onset, running a relatively long course as compared with the acquired form of the disease.

Other Cases in the Literature

Juvenile paresis is itself so rare that its occurrence in a twin must be very rare indeed. A search of the literature as far back as 1906 (the year of the discovery of the Wassermann reaction) has revealed one other case of juvenile paresis in a twin and one case of juvenile tabo-paresis in a twin. Cases of cerebral syphilis, such as Dennie described, have been excluded.

Wile and Welton (1938) described dizygous twin brothers, aged 18 years, one of whom was healthy, the other suffering from juvenile paresis. The twins were a seventh pregnancy and were dissimilar, as evidenced by different iris colour and pigment pattern, different hair colour, and no point of similarity in comparison of foot patterns or fingerprints. Detailed anthropometric observations tabulated in their paper combined with the above evidence to leave little doubt as to the dizygous nature of the twinning. The healthy, non-syphilitic, twin was born 45 minutes before his brother, to whom he was always mentally and physically superior. During the period of one year in which he was kept under observation he showed no clinical evidence of neuro-syphilis; five blood Wassermann reactions were negative ; and one cerebro-spinal fluid analysis was completely negative. The paretic twin was mentally dull and backward from infancy. He had frontal and parietal bosses, peg-shaped upper central incisor teeth, one notched, and anterior thickening of both tibiæ. Central and disseminated chorioretinitis was present in both fundi. Little information is given as to progressive mental deterioration except that he was slow in answering and had difficulty in reading. His pupils were unequal and fixed, he was dysarthric with tremor of the lips and tongue, and both plantar responses were extensor. The blood Wassermann and Kahn tests were repeatedly positive and the cerebrospinal fluid analysis was typical of paresis, viz. : Cells=29 lymphocytes per cu. mm.; globulin=positive ; total protein=0·43 per cent.; Kahn=++ ; Lange curve+5.5.5.4.3.2.1.0.0.0.0.

Blood Wassermann reactions on five surviving sibs were uniformly negative. The father was normal on careful physical examination, and his blood Wasser-

mann was negative on the two occasions on which it was taken. The mother, however, had a strongly positive blood Wassermann, but refused any further examination.

McKendree (1937) described twin sisters, aged 13 years, possibly monozygous, one of whom was healthy, the other suffering from tabo-paresis. This case is of extreme clinical importance in view of the possibility that the twins are monozygous. The twins had similar facial features, like colouring of hair and eyes, and the father said he had seen only one afterbirth. No details of clinical findings in the case of the healthy non-syphilitic twin were given, but the cerebrospinal fluid analysis was negative with a negative Lange curve, and the blood Wassermann was negative, although whether on more than one occasion is not recorded. The paretic twin was always dull and backward and physically smaller than her healthy sister. Semilunar notches were present in both upper central incisor teeth. She was a happy imbecile, dysphasic and dysarthric. There was a right external strabismus. The pupils reacted sluggishly to light and the right was larger than the left. The right ankle jerk could not be elicited. The blood Wassermann reaction was positive and the cerebrospinal fluid analysis showed: Cells=2 per cu. mm. ; globulin=a trace ; W.R. =++; Lange curve=5.5.5.4.3.2.1.0.0.0. Three surviving sibs of the twins had completely negative blood Wassermann reactions. Both parents were known to be syphilitic and the mother had had three miscarriages.

No case of juvenile tabes appears to have been recorded since 1906. Whitmore (1924) described as tabetic mentally defective twin sisters aged 10 years. One had optic atrophy and interstitial keratitis, the other had an Argyll Robertson pupil. In both cases the reflex functions were normal. Both had a pleocytosis in the cerebrospinal fluid and a positive blood Wassermann reaction. The cerebrospinal fluid Wassermann was negative in the twin with the optic atrophy and positive in the other. Whitmore's twins are probably cases of cerebral syphilis and not juvenile tabes as he asserted: a demonstration of tabetic mask anæsthesia in mentally defective children of 10 years old is unconvincing.

These interesting cases of delayed congenital neurosyphilis prove that in twins total escape or mild infection of one twin may occur while the other suffers the full onslaught of the disease. The phenomenon of the escape of the healthy twin is of great speculative interest. In dizygous cases both twins and both placentas must be equally exposed to the maternal spirochætæmia; but it seems that syphilitic disease may affect the placentas unequally or at different periods of uterine life. Why a syphilitic focus should appear in one placenta and not in the other is obscure. In monozygous cases where one placenta has been shared by both twins the apparent escape from infection of one fœtus is even more difficult of explanation.

It is curious and interesting to note the development of paresis in the acquired form in both twins at approximately the same age, as described by Clouston and Savage (1888). They described twin brothers, apparently dizygous, aged 37 years, both commercial travellers. Primary infection appears to have taken place about the same time and the brothers developed paresis at

approximately the same age. The one was admitted to the Royal Edinburgh Asylum under Sir Thomas Clouston and the other to the Royal Bethlem Hospital under Dr. George Savage. Although these cases occurred before the era of serological tests, there can be little doubt from the masterly clinical descriptions given that they were really cases of paresis. In the Bethlem case there was a post-mortem with characteristic findings.

I have to thank Mr. Keith Duff, of the West London Hospital, for information regarding the earlier history of the R. family. To Dr. John H. Ewen, the Medical Superintendent of Springfield Mental Hospital, I am indebted for the cerebrospinal fluid analysis of the affected twin, and to Dr. R. Race, of the Galton Laboratory Serum Unit, for data regarding the blood-grouping of the twins.

REFERENCES

Bergel, A., and Zimmermann, O. (1932). *Med. Klinik.*, **28,** 1668.
Clouston, T. S., and Savage, G. H. (1888). *J. ment. Sci.*, **34,** 65.
Dennie, C. C. (1924). *Med. Clin. N. Amer.*, **7,** 1219.
Friedenreich, V. (1938). *Blood Groups and Genetics* (*Galton Lectures*). *Ann. Eugen.* **8,** 152.
Haslund, O. (1924). *Ann. Derm. Syph.*, Paris, **5,** 321.
McKendree, O. J. (1937). *N.Y. St. J. Med.*, **37,** 659–662.
Menninger, W. C. (1936). *Juvenile Paresis.* Williams and Wilkins Co., Baltimore.
Whitmore, F. (1924). *Minnesota Med.*, **7,** 430.
Wile, U. J., and Welton, D. G. (1938). *Amer. J. Syph.*, **22,** 544–554.

THE ELECTROENCEPHALOGRAM IN ELECTRICALLY INDUCED CONVULSIONS IN RABBITS

BY

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THAT it is easily possible to produce generalized convulsions of short duration in animals with alternating current of high voltage, applied for a short time directly to the intact head, has been known for several years. In 1938 Krasnogorsky reported the influence of convulsions produced by such means on the behaviour of dogs. Spiegel, in 1936, described in detail a method by which one can determine the " convulsive threshold " of an animal. In experiments designed to test the anti-convulsive effect of different drugs, Merritt and Putnam (1938) produced convulsions by using an interrupted rectangular direct current given 80 times per second. The many studies which were undertaken under the auspices of the " Conference on Electric Shock," and were published between 1927 and 1930, are for our special purpose without direct interest; these authors (especially O. R. Langworthy and W. B. Kouwenhowen) investigated the effect of much higher voltages (500–2,000 volts) upon the respiratory, circulatory, and nervous system. The position of the electrodes on the head differed for each author, but apparently played no rôle as to the type of convulsions produced. Krasnogorsky (1938) placed one electrode on the top of the head between the ears and the other under the jaw. Spiegel (1936) inserted them into the conjunctival sacs of both eyes because former experiments had shown that there the resistance was smaller and less variable. Merritt and Putnam (1938) fastened one electrode in the mouth, the other over the occiput. Cerletti and Bini undertook a series of experiments in dogs in which generalized convulsions by essentially the same method as that described by Spiegel were produced. Following these experiments they applied a similar procedure to humans in the treatment of certain psychotic states (Cerletti and Bini, 1938). Since then this method in place of the convulsive treatment with metrazol has been employed in several clinics (Kalinowsky (1939), Sogliani (1939), Müller (1940), Golla *et al.* (1940)).

Before adopting this therapeutic procedure ourselves it was thought advisable to study the physiological processes in these electrically induced convulsions in animals. The electroencephalograph was chosen as the best available indicator of cortical function.

Method

Rabbits were subjected to the following operation under local anæsthesia: skin, muscle, and periosteum were removed from the top of the head over an area of 2 by 4 cm. Six holes were drilled electrically just deep enough to insert fine screws to which the recording electrodes were attached. This was desirable for two reasons. First, it was necessary to ensure that the electrodes did not become loose during the seizures, and secondly, it allowed comparison of the results of shocks given on different days to the same animal. In some experiments a seventh electrode was similarly placed in the occipital bone as an " inactive " electrode for " unipolar " connection. An early attempt to fasten this " inactive " electrode to a place remote from the head, such as the ear or a shaven part of the body, had to be given up because of the interference from muscular action-currents during the seizures. The electrodes, either unipolar or bipolar, were connected through an amplifier system to an ink-writing recorder constructed by Mr. A. M. Grass. As six amplifier systems were at our disposal the electrocardiogram and the muscular action-currents of one fore-leg were recorded simultaneously in many experiments. Owing to disturbance produced by the alternating current, the recording was begun about a second after each shock.

The stimulating or " shock " electrodes were placed directly above the hind-angle of each eye after the hair had been shaved and a small amount of electro-jelly rubbed into the skin. Every effort was made to ensure that these electrodes were as near as possible in the same spot in the different rabbits, and in the same rabbit on subsequent days. Some of the minor differences in the results may be ascribed to slight variation in position of the electrodes. The main supply was reduced by means of a variable transformer (Variac Type 200B), and an X-ray time switch (Type Wappler-Impex) regulated the duration of the current. Under these standard conditions the voltage necessary to produce a generalized seizure lay between 25 and 35 volts, and the duration mostly $\frac{1}{10}$ second. Before each experiment the resistance to alternating current was determined approximately.

During each experiment the animal was tied to an animal-board, and the head immobilized by a Cermak's clamp. An additional bandage had to be put around the mouth in order to prevent it slipping out of the clamp during the initial stage of the convulsion. The convulsion produced had similar characteristics to those described by Spiegel (1936); a detailed description therefore seems unnecessary.

Results

Before each " shock " was given, a control electroencephalogram was taken. In most of our animals the recording electrodes lay over the area præcentralis agranularis, and the familiar response pattern of this area was recorded. When care was taken to exclude as far as possible all outside disturbances, characteristic runs of fast waves were present, sometimes with a longer, sometimes a shorter rhythm. In some of the animals these runs were either never present or they disappeared a few days after the first electroencephalogram had been taken. It was common to find in such a case that either the drill had gone too deep and had injured the surface of the brain or an infection had developed.

The " shock " was then given. With the click of the switch, the animal jumped in its bandage, and then stretched out into an opisthotonus, tail erect, as far as the ties would allow it. Not infrequently fæces and urine were ejected. Within 6–10 seconds this state passed, without marked interruption, into a series of clonic contractions, the number of which varied in the same animal, and from animal to animal. The pupils were wide, the corneal reflex was

absent. When the clonic phase was over, the animal lay with all muscles relaxed and the tail down. Usually slow conjugate oscillations of the eyes from side to side could be observed for a varying time after the clonic phase. During the first tonic state, respiration ceased; the clonic phase was accompanied by inspirations and expirations; later the respiratory rate became rapid but gradually returned to its original rate.

In the electroencephalogram the tonic phase made itself evident by a continuous sequence of large spikes with a frequency of 3–10 per second. Towards the end of this phase the spikes were spaced wider and wider apart and became more triangular in shape (Fig. 1). The clonic phase was marked by a single or double spike, fast in the upward and slow in the downward phase on the

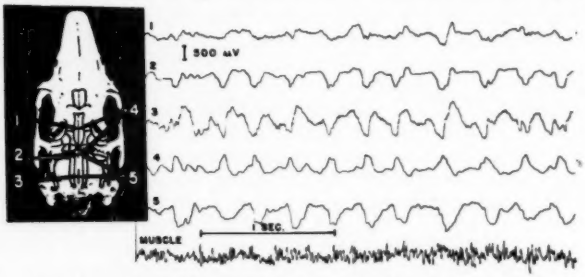

Fig. 1.—30 volts, given for $\frac{1}{10}$ second. 10 seconds after shock. " Tonic " phase.

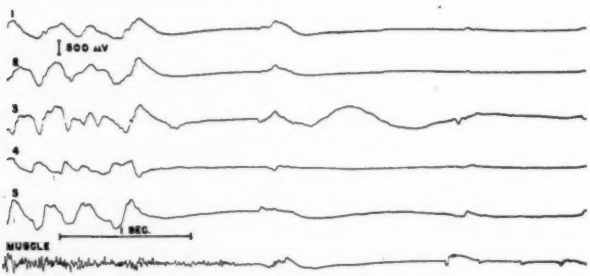

Fig. 2.—The same animal 19 seconds after the shock. The " tonic " phase passes into the " clonic " one.

record. All other fast oscillations had disappeared (Fig. 2). These eruptions were followed by a period in which either all electrical activity ceased and the oscillograph wrote an almost straight line, or slow swings, of low voltage, were present. This latter period lasted from one to several seconds (Fig. 3). From the resulting straight line, slow swings (one per second and less) emerged and became gradually bigger and faster until finally the whole pattern consisted of large 2–3 per second waves (Fig. 4). In some experiments the original pattern was resumed within 1 minute; in others the period of slow waves continued for several minutes (Fig. 5). At this stage every disturbance had to be avoided, even more so than during the control run; otherwise, the slightest noise, e.g. the sliding of the recording paper down to the floor or a whisper between

the experimenters, might instantaneously destroy the fast runs just reappearing and keep the pattern dominated by slow waves only.

During the tonic phase the records from the muscles showed a continuous discharge of large and fast-action currents. Towards the end of the tonic phase,

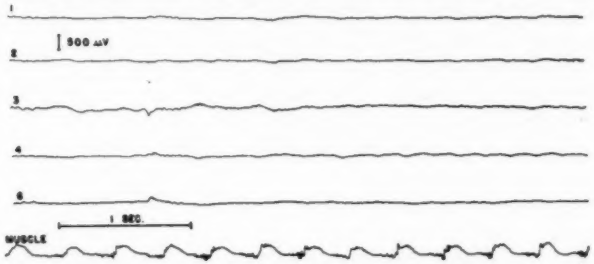

Fig. 3.—Direct continuation of Fig. 2. Notice the clonic discharges in the record from the muscle, while the monopolar and bipolar records from six different points of the motor cortex are almost flat.

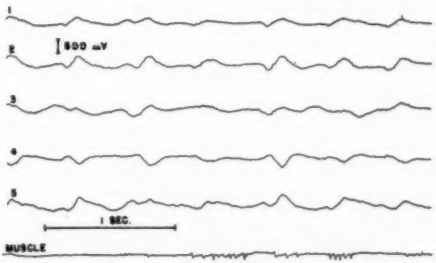

Fig. 4.—57 seconds after the shock. Beginning recovery of the cerebral electro-activity.

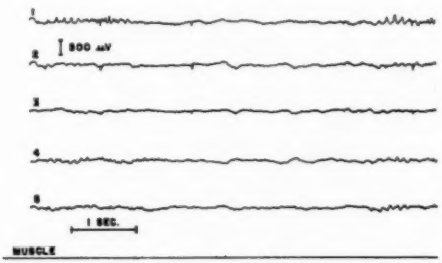

Fig. 5.—First reappearance of the normal activity of the area præcentralis agranularis; 185 seconds after the shock.

these action currents gradually faded out and were almost entirely absent before the first clonic jerk. Each of the cerebral discharges was accompanied by a simultaneous muscular one. But when the brain had ceased to show electrical activity (the " silent period " just after the end of the clonic phase), we observed many times a series of muscular contractions of clonic character which was not accompanied by any cerebral equivalent. This was observed with both

bipolar and monopolar connections. Finally, half an hour after the shock no signs of disturbed electrical activity were to be found in the records. Nor were there any symptoms of abnormal behaviour when the animal was let free from the table. When the animal was freed prior to the full return of the " normal " pattern, it would either stumble from one side to the other, even fall, or it would sit motionless and not move even when pushed.

Occasionally the stimulus, intentionally or accidentally, did not provoke a fully developed convulsion. The clinical picture in such an instance consisted only of one lightning-like contraction of all muscles; thereafter the animal lay quietly but with a more frequent but less deep respiratory rhythm. The electroencephalogram showed slow waves with large amplitude of the same sort as described for the post-convulsive phase in any other type of attack. We never observed a " silent period " under these conditions. It is not possible, however, to exclude with certainty its presence during the short period before the ink-writers were turned on. The fast runs reappeared in the same gradual fashion as in the experiments with long-lasting seizures, but the interval with slow and disorganized waves was much shorter.

Discussion

When we compare our findings with the electroencephalograms during convulsions produced by metrazol, as first described by Fischer and Löwenbach (1934) in animals and recently again by Goodwin, Kerr, and Lawson (1940), by Cook and Walter (1938), and by Rubin and Wall (1939) in man, we note that the records resemble each other closely. The description of the attacks could well be that of an electrically produced seizure. The brain, once induced to discharge its energy explosively, seems to act in the same way regardless of how the explosion is set off. It even seems that the type of reaction is the same for rabbit and cat as it is for man. After a continuous display of maximal activity (successive spikes), the tiring cells appear to fire seriatim at longer and longer intervals (clonic bursts), until final exhaustion prevents all further activity (silent period). Restitution is indicated by the gradual reappearance of at first slow and later faster waves with the final return to the normal activity.

There is, however, one basic difference between the two pictures. When metrazol has been injected, there is a period, sometimes extending up to 10 seconds, during which the amplitude of the curves becomes gradually larger, and the frequency of these mounting waves becomes faster before the salvo of spikes breaks loose. When alternating current is used the peak is reached instantaneously. No latent period is required for the concentration of the convulsive agent to attain its effective level. In the treatment of patients, this point is of great practical importance. It is during this latent period that the patient experiences anxiety and the anticipation of impending danger which so many patients afterwards recall with distress. Moreover, these sensations are not blotted out by the amnesia which comes to cover the time of the convulsion proper. With the electrical method the absence of these sensations, as reported by all authors who have made use of it so far, is explained

by the suddenness of the onset of the cerebral disturbance at the moment the switch closes the circuit.

Cook and Walter, on the one hand, and Rubin and Wall, on the other, disagree on the question whether clonic movements occur without a cerebral electrical equivalent. The former saw clonic contractions of the muscles when the electrical activity of the brain had already ceased. Rubin and Wall, who recorded simultaneously the muscular-action currents, were unable to substantiate this. They believe that the results of Cook and Walter are explained by the fact that the latter used bipolar connections only, and that the straight line in the electroencephalographic record during the clonic phase is a consequence of a strictly synchronous activity of the cortex. We have seen too often the action currents associated with clonic muscular contractions continuing into the " silent period " of cerebral action potentials with monopolar as well as bipolar connections to regard the " silent period " as a fault of the method. We feel sure that at least some of the muscular contractions are not of cortical origin. One might further expect that the huge spikes occurring during the tonic phase would have to be produced by " synchronous " activity in the central nervous system, and that bipolar connections, therefore, would show isoelectrical waves. We think that the tonic state originates entirely in the cerebrum, and is the muscular expression of rapid discharges of cortical centres. The clonic contractions, however, may arise from activity of the nervous system at lower levels, even from the segmental motor neurones—comparable, perhaps, to the muscular twitches after application of strychnine—at a time when the higher parts of the brain are already fully exhausted. This view is in accord with the findings of Samaya (1903), who reported that clonic convulsions may be induced in rabbits and other animals by electrical stimulation of the medulla oblongata. In man, Jasper and Andrews (1936), recording changes in cerebral potentials and muscular action currents at the same time, saw occasionally clonic movements which appeared quite independently from the seizure phenomena on encephalographic records.

In none of our experiments did we find changes of the pattern of changes in cerebral electrical potentials which lasted longer than the clinical picture would lead us to expect. Animals which were given 16 convulsions within 22 days showed much the same " resting " pattern each time before the current was applied. Anatomical studies on the same material have been begun and will be recorded after they have been completed.

Summary

Rabbits were subjected to convulsions induced by 60-cycle alternating current (25–35 volts, usually for $\frac{1}{10}$ second). Cerebral action potential changes were recorded from electrodes fixed in the bone of the skull, with all overlying muscle removed.

In the tonic phase of the convulsions, which came immediately after administering the current, the records showed large spikes, at first in a continuous run (3–10 per second). Then these became spaced farther apart,

until one or more spikes appeared only at intervals, synchronous with the jerks of the clonic phase. Then all significant oscillations usually stopped (" silent period " of cortical activity). However, clonic contractions of the muscles, simultaneously recorded electrographically, not infrequently extended into this " silent period." The changes in cerebral action potential then returned after seconds or a few minutes and went through slowly swinging deflections to arrive gradually at the usual pattern in the course of some minutes to about half an hour.

These phenomena are interpreted as indicating immediate, almost continuous, maximal discharges of cortical cells, then seriatim firing at longer intervals as the cells tire, followed by cessation of all demonstrable activity with exhaustion. The muscular action currents of the clonic twitches may continue into the " silent period " of cerebral exhaustion, so that at least some of the later muscular contractions may arise from discharges originating at lower levels of the nervous system than the cortex.

Preliminary runs were taken before giving each convulsion and occasional records were obtained after the series of 16 convulsions had been completed. During the period of observation no appreciable change could be noted in the records of changes in cerebral action potentials obtained before and after the convulsion.

The main difference in convulsions induced electrically and those produced by metrazol consists in the absence of a latent period and the wider range of duration and severity which can be obtained in the former. Convulsions come immediately after closing the electrical circuit, and the effect may be made much shorter and milder than is possible in a metrazol convulsion.

References

Cerletti, U., and Bini, L. (1938). *Boll. Acad. med., Roma*, 136.
Cook, L. C., and Walter, W. G. (1938). *J. Neurol. Psychiat.*, **1**, 180.
Fischer, M. H., and Löwenbach, H. (1934). *Arch. exp. Path. Pharmak.*, **174**, 502.
Golla, F., Walter, W. G., and Fleming, G. W. (1940). *Proc. roy. Soc. Med.*, **33**, 261.
Goodwin, J. E., Kerr, W. K., and Lawson, F. L. (1940). *Amer. J. Psychiat.*, **96**, 1389.
Jasper, H. H., and Andrews, H. L. (1936). *Quant. Biol.*, **4**, 320.
Kalinowsky, L. (1939). *Lancet*, 1232.
Krasnogorsky, N. I. (1938). *Proc. 15th int. Physiol. Congr.*, 239.
Merritt, H. H., and Putnam, T. J. (1938). *Arch. Neurol. Psychiat.*, Chicago, **39**, 1003.
Müller, M. (1940). *Schweiz. med. Wschr.*, **70**, 323.
Rubin, M. A., and Wall, C. (1939). *J. Neurol. Psychiat.*, **2**, 107.
Samaya, N. (1903). *Trav. Lab. Physiol., Geneve*, **4**, 49. (Quoted from Blume, W. (1926). *Arch. exp. Path. Pharmak.*, **116**, 234.)
Sogliani, G. (1939). *Rass. Studi psichiat.*, **28**, 652.
Spiegel, E. A. (1936). *J. Lab. clin. Med.*, **22**, 1274.

SOCIETY OF BRITISH NEUROLOGICAL SURGEONS

27TH MEETING

Held in Oxford, 18th September, 1940

PRESIDENT : MR. NORMAN DOTT

THE Meeting stood in silent homage to six members who had died : Mr. Wilfred Trotter and Mr. L. Bathe Rawling (former Presidents), Dr. Harvey Cushing and Dr. Thiery de Martel (respectively Emeritus and Honorary Members), Mr. Archibald Young and Mr. A. R. D. Pattison. Forty-five members and visitors attended.

A telegram of greeting was despatched to the newly founded Society of Australian Neurological Surgeons. The programme of their inaugural meeting had been received.

1. Discussion on recent experiences with Gunshot Wounds of the head. (Geoffrey Jefferson.)

GEOFFREY JEFFERSON, in opening the discussion, said that it had been possible to obtain information from some of the special centres and that his remarks would be based on this. Further material would be disclosed as the meeting progressed. The last two decades had brought forth advances in both neurology and in surgery, so that we could surely prophesy that discoveries would be made and interesting new conceptions emerge. Although we looked to the past for guidance, we did so in a very general way, for many of our problems were new. He would refer only to penetrating wounds with dural laceration, leaving to others the scalp wounds (which had once upon a time fascinated him) and the cranial fractures.

G.S.W. HEAD—DURAL PENETRATION

CENTRE	NO. OF CASES	DEATHS	F.B. PRESENT	F.B. REMOVED	C.S.F. INFECTED	FUNGUS	BRAIN ABSCESS	NO OPN.
A	10	0	3	1	0	4	1	2
B	10	3	7	1	1	1	2	5
C	11	1	1	0	2	4	1	1
D	6	0	1	0	0	1	0	0
E	5	1	3	0	1	1	1	3
	42	5	15	2	4	11	5	11

The mortality in the 42 cases was 5 (about 12 per cent.). This was a very low figure. His own mortality in 1918 for this type had been 37·6 per cent.; Cushing's fell from 54·5 for his first 40 cases to 40·9 for the second, and then to 28·9 for the last 45. The speaker would forecast that anything under 20 per cent. would be remarkable, and under 30 per cent. good. There were two chief causes of death, (*a*) the primary injury and (*b*) infection. We could do a little to mitigate the first, but it was in the second group, the later deaths, those at over a week, that we might look to

improve on past mortality rates. As for missiles, rather less than half the cases had an indwelling foreign body and only three times was it removed at operation. In no case where the missile was deliberately left had the retention of the foreign body been an impediment to cure. Members had shown commendable discretion in leaving these metallic fragments alone. None the less, we should be chary of concluding that they never need removal. So far, we had seen very few examples of wounds by high explosive shell, such as were so frequent in the last war. Sizable pieces of steel were best removed with the electro-magnet. The small size of the metallic foreign bodies was another striking peculiarity. Further cases might confirm or correct experience so far on that point. The speaker next referred to wound infection and indriven bone fragments. He had, in the last war, often excised a wound two and three days old if the scalp did not look actively infected and if the wound edges were ragged and devitalized; infection did not spread quickly in the scalp. If the wound of entrance was very small, it would often be left alone. Indeed, in the present series, 26 per cent. had not been operated upon at all. That was because they were punctured wounds, caused by small, high-velocity fragments of bomb casing. Even indriven bone fragments would be left alone if the wound was already sealed and healthy-looking. Encephalograms of one such case were shown which demonstrated traction of the ventricular wall towards a small shower of bone splinters. It was eight weeks after wounding, but, none the less, it was an unexpected happening, because bone fragments were so commonly infected. Arising out of this point, the speaker raised an important question—whence did wound contamination and subsequent infection come? Was it carried by the missile, did it enter from the skin of scalp or face, or did the patient infect it with his hands? Neuro-surgeons might help to clarify these points by making cultures from the wounds, scalp, and fingers of the wounded, as infected clothing and underclothing did not complicate the picture. The good progress of small punctured wounds seemed to imply that surface infection was the most important factor. Larger open wounds needed more active surgical cleansing. Little reliable information was as yet obtainable about the value of sulphonamides like M. & B. 693. The general impression of its usefulness had not yet been raised to statistical certainty, though that very likely would happen. Lumbar puncture had been employed frequently though not all surgeons yet realized how much knowledge would be obtained from it. He referred not only to cytology and culture but to the estimation of albumin. Some reaction in the c.s.f. no doubt occurred in all cases of dural penetration. The course of events was mirrored in the fluid reactions; contusional and very mild inflammatory states showed in the albumin more clearly than in the cell count. The estimation of the extent of parenchymatous damage might be helped in this way. There were 5 late abscesses, a proportion of 1 in 10, a sufficiently high number to make us wary in the after-care of penetrating wounds. Confidence could be felt that members of the Society would make valuable contributions, as time passed, on the prevention as well as the pathogenism and treatment of abscess formations.

WYLIE McKISSOCK said that, in his own cases, the foreign bodies had been very small. He had left them alone because he had felt it improbable that he would be able to discover them at the bottom of such long and narrow tracks. Another difficulty arose in the not infrequent cases where several small pieces of metal were present, and he showed an X-ray of multiple scatter in the parietal region. He had used M. & B. 693; in one case he regretted that he had started it too late (a case developing a late abscess). He had found it difficult to discover whether the patients had had sulphonamide and, if they had, how much.

K. C. EDEN : During the first year of the war, 75 cases of head injury have been treated at Centre F, and of these 35 cases were examples of open fractures and penetrating injuries.

The following analysis is confined to the last four groups in Table I. So far, unfortunately, there has been a considerable delay before the cases have reached us, and in many instances operations had already been performed. The average duration

of the wounds on admission was fifteen days. Some of these cases were from Dunkirk and the delay was unavoidable, but it is to be hoped that as the organization improves the civilian cases will reach us earlier. These figures show that the results have been impaired by the delay and in some instances by inadequate initial treatment.

TABLE II.—ANALYSIS OF RECENT HEAD INJURIES TREATED AT CENTRE F DURING THE YEAR SEPTEMBER, 1939–1940

Concussion without fracture and simple scalp wounds	33 cases
Concussion with closed fracture	7 cases
Open fracture (dura intact)	7 cases
Cranio-facial injuries	3 cases
Penetrating injuries of the brain not involving the ventricles	21 cases
Penetrating injuries of the brain involving the ventricles	4 cases
Total	75 cases

NOTE.—This list includes the figures from Centre D.

The distribution of the wounds of entry is shown in the accompanying diagram.

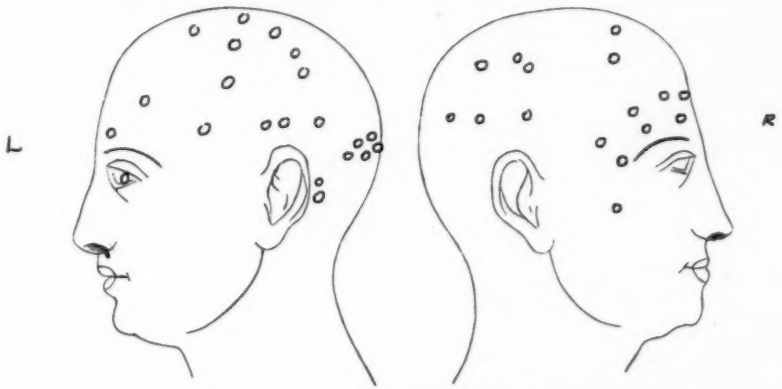

Diagram to show site of wounds of entry in service cases.

No information is available about the number of these patients who were wearing steel helmets at the time of the accident, but it is interesting to note that many of the wounds were low in the frontal region or in the occipital or mastoid area.

M. & B. is known to have been given to 13 out of 35 cases before admission, but it is impossible to say whether the dosage was adequate or whether others had it also.

Half of the cases admitted to hospital had infected wounds or wounds healing by delayed union. Fragments of bone were present in all the tracks which had penetrated the dura and in a considerable number small pieces of metal were present.

It is surprising to note the number of cases with wounds not involving the dura which were complicated by signs of intracranial damage to the nervous system. In one of these cases there was a careful note of the condition of the dura at operation, which was carried out in France, and the wound was healed on admission. In this case, although the dura and underlying brain appeared quite normal, there was a profound hemiplegia, which was still recovering slowly when the patient was discharged from hospital.

The cerebrospinal fluid was examined in all the cases of wounds penetrating the dura which were admitted to the hospital at an early stage. Three of these showed a positive culture of mixed organisms (staph, coli, and strep). In 14 other cases which

were examined, 8 showed a slight reaction in the c.s.f. in the form of increased protein or cells.

M. & B. was given to all fresh perforating injuries. It is impossible at this stage to assess its value, but the general impression is that it was of assistance in preventing meningitis. It failed to save 3 out of 6 patients with established meningitis, but in one case which had an area of non-suppurative encephalitis around buried foreign bodies with a c.s.f. containing 17 cells/cu. mm., and 0·12 per cent. protein, the fluid rapidly became normal with M. & B. therapy.

In spite of the number of foreign bodies present and the proportion of wounds which healed by delayed intention only one patient, a case with a track penetrating the dura, had a fit while in hospital. It is still too early to obtain any information about delayed fits.

Cerebral fungus was present in 6 cases of injury to the brain substance. They were all associated with buried fragments of bone and suppurating or granulating wounds. In some cases the brain was explored and small pockets of pus and fragments of bone removed, and in all instances the brain receded and the wound healed when the infection subsided.

Five cases developed abscesses, 3 of which communicated with the ventricle, and these were all fatal. Two cases developed meningitis unassociated with abscess formation, but in neither case was it fatal.

There were two examples of cerebrospinal fistulæ, both with cerebrospinal rhinorrhœa, and one with a large aerocele. The fistula was repaired by operation in both cases.

With regard to the operations performed at this hospital only 3 cases of penetrating injury to the brain were received early enough for excision of the wounds and debridement. The chief problem was how to deal with the open infected wounds containing foreign bodies. Seven of these cases were explored, foreign bodies removed, and abscesses drained, and 4 of these were fatal. Of the remaining cases, which were left alone, all but one healed in the end without fatality. As a result of this we are inclined to treat these cases conservatively.

With penetrating injuries of the brain not involving the ventricles the prognosis is surprisingly good, and there was only one fatality in this series. This patient had an infected wound five days old containing several large pieces of wood, which were removed at operation. He subsequently developed an abscess and meningitis which proved fatal. There is no doubt, however, that most of the complications could be avoided if the wounds were adequately debrided and sutured at an early stage. In contrast, the perforating wounds involving the ventricles all proved fatal in spite of M. & B. therapy. Two of these had infected tracks leading into the ventricle, one had an abscess opening into the ventricle, and one had a massive intracranial hæmorrhage. The cranio-facial wounds were very painful and there was prolonged suppuration in each of the 3 cases, but all healed in the end without complication.

The improvement in the c.n.s. signs was encouraging in all the cases which recovered. Those with slight degrees of paralysis recovered completely in a few weeks, while there has been a marked improvement even in the most severe cases. Several cases with hemianopia have all shown progressive improvement, and others with varying degrees of aphasia have all shown a tendency to improve.

Recently we have made use of a mobile surgical team to deal with civilian air-raid injuries, and the results so far have been very encouraging. All the cases have been dealt with in twenty-four hours or less from the time of the injury, and in each case debridement and primary suture of the wounds has been carried out. Bone fragments have been removed in each instance, and in 2 cases the splinters of metal have also been extracted. Three cases were comatose with deeply penetrating tracks, and these died without recovering consciousness; the remaining 5 cases are improving steadily and their wounds have all healed by primary intention.

HUGH CAIRNS : At Centre G we have had 29 cases of G.S.W. head, and of these

3 have died. The fatal cases were (1) a case of brain abscess after scalp wound ; (2) a case of fulminating meningitis after a penetrating wound of the ventricle ; and (3) a case of delayed meningitis after an inconspicuous penetrating wound of the brain through the frontal sinus. Among 9 cases of simple scalp wound there were 2 serious cases of delayed intracranial infection, one a fatal case of brain abscess following infection of the scalp wound and focal osteomyelitis beneath the wound, the other a case of local subdural abscess beneath an infected scalp wound in which the patient was almost moribund at the time of admission. These cases show the danger of infection of gunshot wounds of the scalp. It appears that after gunshot wounds of the scalp the underlying tissues are more damaged and more vulnerable to the spread of bacterial infection than they are after the scalp wounds of civil head injuries. In these circumstances surgical cleansing, excision, and suture of scalp wounds after battle is by no means a trivial operation, but should be performed with all the care of a major operation: it should be regarded as the most important cranial operation of war.

In comparing this series of head injury with the closed head injuries of civil life certain differences call for comment. In this series by far the greater number were not unconscious, or only momentarily dazed, at the moment of injury. The only cases of severe loss of consciousness were wounds involving the base of the brain. Thus one man with a fragment of metal passing in through the external auditory canal to lodge in the cerebellar vermis was unconscious for several days; others with similar pieces of metal damaging the occipital lobes were not unconscious at all. Detailed study of the situation of brain damage in patients rendered unconscious by missiles may throw some light on the cause of concussion.

In scalp and skull wounds without penetration of the dura there is often evidence that the brain is damaged, either sensory-motor signs of the type described by Jefferson after the last war, or homonymous field defects, as described in the last war by Montagu Hine. In another case of scalp wound from a bullet or bomb fragment the patient did not lose consciousness and showed no neurological signs, except diminished tendon jerks ; nevertheless, the patient had free blood in his cerebrospinal fluid. Brain damage thus occurs in non-penetrating gunshot wounds of the head. In this limited series of cases the evidence is that it is present in a relatively narrow zone beneath the point of impact. The only cases of civil head injury that show similar focal injury are those due to violence applied over a very small area, as by a golf-ball, cricket-ball, etc.

Spontaneous recovery from penetrating injuries may be remarkably complete: severe hemiplegia and aphasia may subside completely after two weeks. These cases frequently make a more rapid return to normal than closed head injuries of civil life.

Information is still needed about the latest time at which primary excision of wounds can be undertaken without aggravating infection. Experience on this problem will be strengthened if it includes thorough bacteriological study of all wounds (and cerebrospinal fluid) before and after wound excision, together with accurate records of sulphonamide treatment. So far sulphonamides appear to have been given in a haphazard manner, and it is impossible to form any accurate impressions of their value.

G. C. KNIGHT said that he could add a series of cases which he had had the opportunity of treating. They consisted of 14 cases of gunshot wounds of the head; only one patient died. Ten had penetrating wounds of the dura, and in 9 metallic foreign bodies were retained (2 removed). The only death was one in which a small piece of bomb fragment had penetrated from the vertex traversing the corpus callosum and third ventricle, and involved the floor of the hypothalamus. This case was of particular interest, for the entry wound was so small that it had been missed on clinical examination and the patient was sent to the Centre as a case of closed injury. He survived for four weeks without any evidence of infection, but during that time

remained in a light coma and showed progressive wasting, suggesting a central metabolic disturbance without any localizing signs detectable in his nervous system.

In the remaining cases he had been most impressed by the value of M. & B. in checking infection when the dura was open. All the cases of which he had charge arrived three to five days after receipt of their injuries, and in 10 of them infection of the wound was already established, in some cases being gross. He would quote three examples which he believed to illustrate the value of M. & B. treatment.

The first, *G. B.*, had the right squamous temporal bone apparently torn away from the skull, as there was no bone driven in; the mechanism of this injury is hard to understand. The dura was open over an area of 4 cm. and the brain billowed in and out of this opening, the cerebrospinal fluid escaping. He had had no treatment other than a field dressing applied over this injury. He came in three days later, having been given M. & B. regularly during transit. There was a slight reaction in the cerebrospinal fluid, but under the full course of M. & B. the wound granulated satisfactorily and was dry and healed within three weeks.

The second case was admitted five days after the injury with an extensive gunshot wound of the left occipital region from which a necrotic fungus protruded which was black and stinking. There were more than eight small metal fragments dispersed widely inside the skull. The cerebrospinal fluid showed well-marked evidence of infection and had a positive culture of staphylococci. Three days after admission the fungus sloughed off. The ulcer on the surface of the brain was below the level of the dura. The cerebrospinal fluid escaped over this and must have washed infection widely over the inner surface of the dura. He developed at this time a right hemiplegia in addition to his previous signs of aphasia and hemanopia. The condition appeared hopeless, but a second full course of M. & B. was given. His temperature fell; the cell count fell; but the protein remained high. Within five weeks his wound was completely healed and he had now recovered from his aphasia and hemiplegia, with no disability other than weakness of the right hand and hemanopia. The protein in the cerebrospinal fluid did not fall until the fungus was epithelialized.

The third case was seen on the sixth day after his injury, a penetrating wound from the right occipital region, the metal traversing the falx and lying in the left cerebral hemisphere. He had at this time a definite streptococcal meningitis. Under M. & B. treatment the cultures became sterile in the c.s.f. in two days, but the protein remained high and rose still further. Five weeks later he developed right-sided Jacksonian epilepsy with a right-sided hemiparesis, evidencing an abscess around the retained metal on the left side. He did not want to operate on the abscess at this time. A second course of M. & B. was given. His temperature subsided and his fits decreased, but increasing hemiparesis and a further rise of protein showed that the abscess was continuing to develop. After three weeks he operated through the left hemisphere and attempted to remove the piece of metal with a magnet, but despite good contact the metal would not lift; it proved to be some form of aluminium alloy. It was therefore necessary to carry out a cone excision. It is interesting that cultures from this abscess show that bacillus proteus was present.

He was convinced that none of these three patients could have survived prior to the introduction of chemotherapy, and he therefore felt that a full course of M. & B. should always be given in penetrating wounds of the head without waiting for evidence that intracranial infection had in fact occurred.

One other point occurred to him—that, with the exception of the penetrating injury involving the vertex, referred to in the first case, the entry wound in every one of his cases lay below the rim of the steel helmet—in the majority, in the right occipital region. It therefore was pertinent to enquire whether the British model was as efficient as it might be in providing protection for the back of the head. The man is standing up. Fragments from a bomb come from ground level, i.e. they strike upwards. One can clearly see in the X-rays that much of the metal had passed in an upward direction from its point of entry. Could not some form of nape extension be provided, possibly consisting of metal slats secured on a leather flap, rather like the old form of Chinese armour ?

S. E. A. O'CONNELL: Professor Paterson Ross had been worried as to what to do in cases of perforating wounds of the brain coming for treatment over forty-eight hours after reception of the wound. One case which seemed to help to answer the problem. A man was admitted with a perforating wound of the right frontal region through which the cerebrum protruded, he had received the wound three days previously. He was treated by scalp excision, skull excision, and excision of the brain track by suction. His wound healed

by first intention, but whereas on his admission he had shown only a paralysis of his left arm, within four days he had a left hemiplegia. The wound was therefore re-opened and an abscess searched for without success; the wound was left open and the case treated as a cerebral fungus. Following this his neurological signs completely cleared up and he left hospital free from symptoms. This had led them to the belief that a perforating wound with exposure of the cerebrum seen forty-eight hours after the reception of the injury should be treated as a cerebral fungus, no attempts should be made to treat it in the same way as a fresh brain wound.

A point that has interested them had been the cerebrospinal fluid in cases of cerebral fungus. In almost all the cases the protein had been greatly raised, in one case to 375 mgms. per cent., whereas the increase in the cells had been very slight. As the cerebral fungus epithelialized, the cerebrospinal fluid protein fell. The reason for this disassociation of high protein and pleocytosis is not clear.

As regards the question of removal of deeply placed foreign bodies in the brain, this on the whole had not been attempted, in the hope that the F.B. might be productive of no harm. If a cerebral abscess should form around it, it would perhaps be better to delay treatment entirely, until the abscess was well encapsulated. However, the matter has occasioned some worry in view of their experience with F.Bs. in the soft tissues of the limbs. Here, of course, the fragments are usually much larger, but often after a prolonged search the situation of one of these F.Bs. has been revealed by a rush of foul fluid along a probe which has entered the small abscess cavity around the F.B. It is to be hoped, however, that the smaller F.B. in the brain will not be so likely to produce an abscess.

D. W. C. NORTHFIELD, referring to some recent cases of his own, asked whether opinion would favour the use of a flap instead of a local nibbling operation. He had tried the two methods and was impressed by the better control and exposure that was afforded by the flap. He had found hæmorrhage occasionally troublesome. It was in his view the only technical difficulty. He had lost one case from bleeding in a deep wound track, so deep that he could not secure the vessel. He asked about the sterility of powdered M. & B., wondering whether it lost its properties under heat.

E. A. CARMICHAEL enquired whether there was any unanimity of opinion as to the value of the sulphonamides and, if so, by what methods should they be administered. The makers put up the product in sterile ampoules; there was no difficulty on that score. He also made some enquiries relative to the protection afforded by the steel helmet. Further, how many of the missiles were magnetic?

S. ZUCKERMAN said that non-magnetic foreign bodies must exist, for the tail-fins and some other parts of bombs (but not the casings) consisted of non-magnetic alloys. He went on to describe the physical behaviour of small metal splinters, travelling at great velocity. He spoke of the heat generated at the compression cap of sound waves forced to travel at more than their normal speed. The velocity reached might be in the nature of 3,000 to 4,000 feet per second when a heat of 200 to 300° C. was reached. The missiles must, therefore, be sterilized in their flight. He outlined experiments which were being undertaken to elucidate the question of sterilization and re-infection of missiles in their transit.

J. HARDMAN wondered whether the advice given by Harvey Cushing in his classical paper, that the intact dura should be opened and contused brain sucked out, should be followed. It seemed to him that, in view of the great difference in mortality between head wounds with open and closed dura, it was a difficult decision.

GEOFFREY JEFFERSON in reply said that the mortality had not been materially altered by the new cases added in the discussion. These totals showed that there had been 10 deaths in 75 cases (13·5 per cent.). He was obliged to Mr. Northfield for having raised the question of the bone flap. He thought it advisable whenever the time needed for it could be found. In a great rush of work it would be impossible. But, as Mr. Dott had remarked privately to the speaker, the principle was similar to that of abdominal surgery, a larger or smaller incision and exposure was to be fitted to the depth of the wound. The bone flap would probably be used more in present-day neuro-surgery of wounds, but not invariably; in the last war it had been little favoured. It was clear that much of value would be added by study of the means and nature of wound infection and on the potency of chemotherapy. More consecutive studies of the c.s.f. would also enlarge our knowledge of the progress of brain wounds.

2. Experimental peripheral nerve injury. (J. Z. Young.)

J. Z. YOUNG gave an account of his experiments on nerve regeneration after section, both alone and with grafts of various kinds. He estimated the rate of growth from the central cut stump at 4·0 mm. a day. This was based on the occurrence of reflex action on pinching the re-exposed nerve. There was considerable delay in functional recovery. Thus, although an axon might be expected to arrive at a muscle in twenty-five days, it was forty-seven days before voluntary movement was possible. There was, therefore, twenty-two days' delay at the motor end-plates. Delay at the

skin he estimated at about a month. He had found no deterioration in the ability of the central and peripheral stumps to give and to receive nerve fibres, even after deliberately delayed " plasma suture." The delays, however, were short (some two months only). He gave evidence that a reciprocal tropism was involved, not only in the outgrowth of nerve fibrils from the central stump, but also in the growth of the Schwann bands from the peripheral stump. He referred further to the very successful experiments made with auto-grafts, and emphasized the uselessness of homo- and hetero-grafts. Details of this work had already been published.

E. D. ADRIAN reminded listeners that the estimated growth of the human axon was only 1·0 mm. a day. He asked what methods Mr. Young had used in estimating axonal progress.

J. Z. YOUNG replied that it was by the eliciting of reflexes by pinching the nerve.

E. D. ADRIAN said that in human beings Tinel's sign had been useful, and enquired how the return of skin sensation had been explored.

J. Z. YOUNG said that it was by the production of movement on mechanical stimulation. He thought that the excellence of the nerve bed in experimental work might explain the more rapid regeneration in animals, though it might be a characteristic of the animal.

J. G. GREENFIELD enquired as to the size of the grafts. He thought that important, because his experience of large grafts in the last war and after was that they were unsuccessful and showed heavy fibrosis histologically. J. Z. Young's grafts were small and lay in undamaged fascial planes.

H. PLATT spoke of the rate of human regeneration, which must certainly be much slower than that in the rabbit. Taking the musculospiral (radial) nerve as the best example, there was often long delay.

J. Z. YOUNG thought the delay might be at the end-plate and not in the nerve trunk.

G. R. GIRDLESTONE believed that what was true of small grafts was not applicable to large. He asked whether there was any appreciable check at the distal line of suture.

J. Z. YOUNG replied that his grafts had not shown it, but that they were not very long (2 cm.). There was no check.

3. Brain fungus. (H. W. B. Cairns, Peter Ascroft, and R. Hannah.)

H. W. B. CAIRNS spoke of the work done on brain fungus by himself in collaboration with P. B. Ascroft and R. H. Hannah. It is seen often after incomplete operations on brain abscess and other intracranial infections, also after penetrating gunshot wounds. The most important single cause is an unclosed opening in the dura. Most cases of brain fungus result from surgical operations, and this statement is probably just as true for fungus with gunshot wounds. Histological studies of human and experimental brain fungus show that the essential changes are : (1) necrosis or degeneration of the exposed brain and the cone of subjacent white matter ; (2) invasion of the fungus by connective tissue ; (3) the glial reaction is inconspicuous. Infection from without may occur along the sulci which are still patent, but fungus itself is not an infective process. Fungus may occasion a rise of the protein content of the cerebrospinal fluid; examination of the cerebrospinal fluid does not help to distinguish between simple fungus and fungus with abscess.

It is a mistake to imagine that a bulging fungus is due to an underlying pathological lesion. Occasionally there is an abscess in the fungus, but more often the primary expanding lesion is at some distance. Generalized hydrocephalus occurs as a complication of fungus, and may cause the fungus to continue to bulge after the primary cause of the raised intracranial pressure, as, for example, an abscess, has subsided. The best method of investigating the cause of brain fungus is by ventriculography. The fungus itself should never be needled unless ventriculography has shown an expanding lesion in or near the fungus. Lumbar puncture is useful to control the size of fungus in the early stages, but should be used sparingly in the late (healing) stage, as it may encourage waves of meningeal infection.

W. CONE had been most interested in this presentation which was a new one. He saw now that it was a self-propagating process, and had been interested in the histological sections which illustrated the paper.

GEOFFREY JEFFERSON objected to the statement that infection played little part in cerebral fungus. If a non-infective basis was insisted upon, what name was to be given to the

acute, heavily-infected wound with brain tissue protruding through the scalp wound ? He entirely agreed that, in the quieter stages or types, with which the previous speaker had dealt, infection was no longer the dominating feature. In this the exposition had been of the highest value. But a parallel could be drawn between, on the one hand, loss of tissue in the limbs and, on the other, in the skull and its coverings. In both an ulcerated surface was the result, and it was a useful pathological conception to regard a cerebral fungus as an ulcer. It could not be maintained that infection played no part in it, even if it was true that severe infection had not always caused it, any more than infection always was the cause of an ulcer or unhealed surface elsewhere. He was convinced that infection was inseparable from the conditions in which fungus arose, though the infection was sometimes secondary. The fungus healed as best it could by fibrosis and epithelialization. There was, perhaps, a bar to healing in the early stages, at the point where mesoblastic tissue encountered brain, with its protection by " insulation." (Trotter.)

J. G. GREENFIELD disagreed with these views, thinking that necrosis was produced by the pressure of the bone edges on the cortical capillaries and that this led to anæmia and difficulty in healing.

DICKSON WRIGHT described his method of treating cerebral fungus by skin grafting, holding the graft in place with a marine-sponge. He strongly advocated this procedure.

CLARK-MAXWELL thought that skin grafts formed the ideal dressing for these cases. He simply washed the fungus well and applied the grafts to the granulations. In 3 cases he had not needed to repeat the operation.

JAMES HARDMAN described a case in which he had ligatured a pedunculated fungus with subsequent rapid healing. In a second case a fungus formed after excision of a thick-walled abscess. The patient finally died; at post-mortem he found ventriculitis and meningitis, indicating that the fungus and the eventual fatality were due to obstructive hydrocephalus produced by the original meningitis.

4. Technique of cisternal encephalography. (J. Schorstein.)

J. SCHORSTEIN reported on a series of over 60 encephalographies performed by suboccipital puncture and found that in 50 cases there had been 10 per cent. failures, whilst in an equal amount of lumbar encephalographies the failures had been 20 per cent. Schorstein described the technique and pointed out that recently he had given up injecting gas and instead only removed the fluid, 10 c.c. at a time. He discovered that injection was unnecessary since air was aspirated if the needle end was left free. The speaker went on to discuss the means by which air was able to enter the ventricle. He agreed with Jüngling that without pulsation and respiratory movements of the brain air would not enter. He had confirmation of this by hearing air entering intermittently. In 3 cases, no fluid was obtained on cisternal puncture, and these cases at operation proved to be posterior fossa tumours in which the cistern was occluded by tonsilar herniation. In a normal person he removed 50 to 60 c.c. of fluid, and that was about the quantity of c.s.f. contained in the skull. There were no deaths in the series, and even the posterior fossa tumours were not made worse. (*This paper will appear later in full.*)

JAMES BULL said that he had seen the method used in Stockholm, where they replaced only 30 c.c. of fluid with gas, and that the impression in Stockholm was that you did not get good surface filling with cisternal encephalography. They had done many thousands of cases by this method without complications and the percentage of failures was the same as in the series presented by Schorstein. In Stockholm it had been suggested that a further 20 c.c. of air should be injected by the lumbar route, with the patient lying down in order to get filling of the sulci and cisterns.

D. W. C. NORTHFIELD questioned the advisability of using a procedure which certainly had its dangers, from injuries both to the vessels and nervous elements in the posterior fossa, while it was still doubtful that the method gave better results than lumbar encephalography. He himself always felt anxious about performing cisternal puncture.

GEOFFREY JEFFERSON asked whether the suction noise could also be heard if the same method were used in lumbar puncture and, although he admitted that there was a theoretical danger in cisternal puncture, he thought that in expert hands it was a perfectly safe procedure. He thought it was unlikely that the posterior-inferior cerebellar artery would ever be lacerated. He believed that the people in Stockholm had got bad filling of the sulci and cisterns because they injected a fixed quantity of air and that a good filling could be obtained if sufficient air was injected.

J. E. A. O'CONNELL asked whether, with cisternal punctures, patients had less discomfort, and said that he himself had always performed encephalography under anæsthesia.

J. SCHORSTEIN, in reply, said that he had seen as good, if not better, surface filling in cisternal encephalography as with the lumbar method. He did not use a fixed quantity of gas, but removed as much fluid as could be obtained (it was always more than 30 c.c.), and allowed air to be aspirated until the intracranial contents had found their own pressure equilibrium. He also thought that this method caused less discomfort to patients, but he had not, as a routine, performed encephalography under general anæsthesia, although he admitted the desirability of doing it. Only once during lumbar puncture had he heard a sucking noise, and that was after very complete withdrawal of fluid.

5. Pontine hæmorrhage as an irrevocable cause of death following episodes of acute hypertension. (Norman Dott.)

NORMAN DOTT described 4 cases in which crises of high intracranial pressure had led to fatality because of pontine and mid-brain hæmorrhage. In the first case a frontal meningioma was operated upon after ventriculography and the session broken off, it was thought, with safety. Blood-pressure was 120/80. The patient failed to recover consciousness from nitrous-oxide anæsthesia. Five hours later the wound was re-opened, the dura incised, but without benefit, and the patient died in thirty-six hours. Post-mortem revealed that there was infarction of the brain-stem. The important factor, he felt, had been the rise of intraventricular pressure by the pneumography, the production of œdema, and probably a further rise of pressure with the induction or continuation of the anæsthetic. He went on to describe three other examples. These hæmorrhages had been described by Moore and Stern, but what interested the speaker was the causation, since no existing theory was adequate. The supposed rise of blood-pressure which some had postulated had not occurred in his own cases. He believed that the explanation was to be found in vascular spasm with damage to the wall of the vessels beyond, diapedesis into and through the walls, and thrombosis. This put the condition in line with what was believed to happen in hyperpietic states. Pathologists had been forced to invoke spasm as a cause of the vascular changes. General anæsthesia might be important in precipitating this condition, and as a result of his experience with these cases he thought it was a wise thing to avoid it in severely compressed cases, in those which had been left just that shade too long before operation.

6. Injuries of the trigeminal nerve. (Geoffrey Jefferson.)

GEOFFREY JEFFERSON said that during the war of 1914–1918 he had observed examples of injuries, not only of the peripheral divisions of the trigeminal nerve but, in two instances, of the ganglion itself. A further example of trigeminal injury had presented itself recently. Injuries of the divisions were commonly found in facial wounds. The ganglion contusions or destruction were rarer and more interesting. Besides his own three cases, there appear to be only three others in the literature where all divisions were affected. It is not generally known that many examples (some 30) have been reported in cases of fracture of the cranial base. He believed that sheath hæmorrhages must be common, for the fracture line in the middle fossa usually passed beneath the ganglion on its way to the pituitary fossa. Some headache and soreness of teeth and face were probably due to ganglionic disturbance. He described an example of damage to the second division at the foramen rotundum and showed a diagram of the sites of election for injury in the course of trigeminus and its divisions.

EPITOME OF CURRENT JOURNALS

AMERICAN JOURNAL OF PSYCHIATRY

Vol. 96. No. 5. March 1940.

*Psychiatric Approach to the Treatment of Epilepsy. S. Cobb. 1009.
*Further Experiences with the Use of Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Disorders. H. H. Merritt and T. J. Putnam. 1023.
*A Comparative Study of the Effectiveness of Dilantin Sodium and Phenobarbital in a Group of Epileptics. J. Weinberg and H. H. Goldstein. 1029.
*A Follow-up Study of Non-Luetic Psychotic Patients with Abnormalities in the Spinal Fluid. P. Solomon, R. S. Schwab, and L. Maletz. 1035.
Dementia Paralytica Accompanied by Manic-Depressive and Schizophrenic Psychoses. D. Rothschild. 1043.
*A Case of Partial Bilateral Frontal Lobectomy. I. C. Nichols and J. McV. Hunt. 1063.
Social Psychiatry—Our Task or a New Profession. S. W. Hartwell. 1089.
Psychoses with Myxedema. R. M. Crowley. 1105.
Behaviour Differences in Mentally Retarded Children measured by a New Behaviour Rating Scale. A. A. Strauss and N. C. Kephart. 1117.
*The Control of Normal and "Convulsive" Brain Potentials. R. W. Gerard and B. Libet. 1125.
Insulin Shock Treatment of Schizophrenia. F. G. Halpern. 1153.
Clinical Observations in the Insulin Treatment of Schizophrenia. J. P. Frostig. 1167.
Psychiatric Facilities in Cincinnati and Ohio. 1191.
Insulin Therapy of Schizophrenia in the Elgin State Hospital. G. Heilbrunn and R. Sternlieb. 1203.
*Neuropsychiatric Disorders Occurring in Cushing's Syndrome. N. S. Schlezinger and W. A. Horwitz. 1213.
Hereditary and Environmental Factors in the Causation of Manic-Depressive Psychoses and Dementia Præcox. H. M. Pollock and B. Malzberg. 1227.

Epilepsy.—Conditions known as epilepsy and hysteria are defined and the existence of "hystero-epilepsy" is denied. True epilepsy is divided into two main groups: (1) familial and (2) due to cerebral lesion. Hysteria occurs usually in women of immature personality and its essential symptoms are conversion and amnesia. It is found that in true epilepsy increased use of the intellectual faculties decreases the number of fits, hence importance of occupation therapy. Cases are described which were treated by different methods; the best results were obtained by psychotherapy. Tables are given. (H. de P.)

Convulsive Disorders — Treatment by Dilantin Sodium.—A report on 267 cases, 144 of which had been previously reported on, treated by dilantin sodium. All had had other forms of treatment previously. Dosage and toxic effects are described and investigation continues. (H. de P.)

Comparison of Dilantin Sodium and Phenobarbital in Epilepsy.—In a group of 15 cases of idiopathic epilepsy with an average duration of 15·6 years, dilantin sodium was gradually substituted for phenobarbital. Results were satisfactory, though some complications occurred. (H. de P.)

Non-Luetic Abnormalities in Spinal Fluid.—165 patients were investigated in whom no organic cause for the abnormality had been found at a previous examination. In 42 per cent. the abnormality remained unexplained; in 54 per cent. organic disease was confirmed or discovered, of which the most common were cerebral vascular disease and chronic alcoholism. It is suggested that the effects of alcoholism and drug-addiction should be further investigated. (H. de P.)

Frontal Lobectomy.—Cases are described which have survived this operation and which show a wide variation in symptomatology. One case is described in detail with the tests used after removal of a frontal lobe tumour in a man of above average intelligence who showed good response to instruction, but lack of initiative and tendency to stereotypy. It is noted that psychosurgery is the substitution of one disease for another, and suggested that frontal lobectomy destroys the "ability to organize life at a normal cultural and intellectual level." (H. de P.)

Changes in Rhythm of Brain.—Experiments were carried out on the isolated olfactory bulb of the frog. When removed from the body the rhythm improves in amplitude and regularity. Its maintenance depends on a steady flow of energy, which is supplied by the metabolism of the cell. Separate factors controlling brain potential are analysed, and the problem of unification of the beat of many cells discussed. Electrical currents can spread through the brain either by nerve impulses or by electric fields. These functions may be applicable to brain function in epilepsy. (H. de P.)

Cushing's Syndrome.—A case of Cushing's syndrome with psychotic symptoms of depression is described. It is suggested that such symptoms are not uncommon in this condition. The case described was not typical and showed also extra-pyramidal neurological signs. There was a suggestion

of chronic encephalitis, which is not commonly found. It remains in doubt whether the mental symptoms are directly due to hypophyseal dysfunction or to associated dysfunction of other endocrines. (H. de P.)

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Preliminary Analysis of Grouping Behaviour in Patients with Cerebral Injury by the Method of Equivalent and Non-Equivalent Stimuli. W. C. Halstead. 1263.
Syphilis in Serum Negative Feeble-minded Children. C. E. Benda. 1295.
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Psychoses Resembling Schizophrenia occurring with Emotional Stress and Ending in Recovery. H. A. Paskind and M. Brown. 1379.
Bioelectric Responses in Metrazol and Insulin Shock. J. E. Godwin, W. K. Kerr, and F. L. Lawson. 1389.
The Effect of Metrazol Administration on Prolonged Refusal of Food in the Psychoses. S. Androp. 1407.
Unsuccessful Sex Adjustment in Marriage. S. B. Wortis. 1413.
The Mechanism of Fractures of the Vertebral Bodies. A. M. Rechtman. 1429.
Mutism and Resistance Behaviour in Psychotic Patients. C. W. Darrow and A. P. Solomon. 1441.
Metrazol as a Diagnostic Aid in Epilepsy. H. H. Goldstein and J. Weinberg. 1455.
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Prognostic Criteria in Dementia Paralytica. M. H. Greenhill and M. Yorshis. 167.
A comparative Study of Thinking in Schizophrenic Children and in Children of Preschool Age. J. L. Despert. 189.
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*Personality Changes accompanying Cerebral Lesions: (i) Rorschach Studies of Patients with Cerebral Tumors. M. R. Harrower-Erickson. 859.
*Vascular Bed of the Retina in Mental Disease. J. M. Cotton, N. D. C. Lewis, and A. W. Egenhofer. 891.
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*Serum Protein, Nonprotein Nitrogen, and Lipoids in Schizophrenic and Manic-Depressive Psychoses. E. F. Gildea, E. B. Man, and R. W. Biach. 932.
*Histologic Changes Following Metrazol Convulsions, with Note on a Fuchsinophilic Reaction as an Index of Early Neurocytologic Change. H. Cleckley, L. Bowles, and F. A. Mettler. 948.
*Temporary Arrest of the Circulation to the Central Nervous System: (ii) Pathologic Effects. L. M. Weinberger, M. H. Gibbon, and J. H. Gibbon. 961.
*Certain Aspects of Defects of Recent Memory occurring in Psychoses of the Senium. D. E. Cameron. 987.
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Status Epilepticus as a Complication of Metrazol Convulsive Therapy. N. G. Becker and S. I. Stein. 993.
The External Geniculate Bodies: Degeneration Studies following Occipital Lobectomy. W. J. German and B. S. Brody. 997.
Cessation of Epileptic Seizures and the Electroencephalogram. R. Osgood and L. J. Robinson. 1007.

Personality Changes in Cerebral Lesions.—Examination of the Rorschach records of patients with cerebral tumours has shown that both as composite pictures and as individual records they differ markedly from the normal. Twenty-eight records of 25 patients with tumours of the brain, even when expressed in graphic form only, show restricted and constricted personality, extraordinarily uniform when contrasted with the variety found in the records of the normal subjects. (R. M. S.)

Vascular Bed of Retina.—The cross-sectional area of the vascular bed of the retina has been measured in a group of psychiatric patients classified as having either schizophrenia or manic-depressive psychosis. It is believed that these measurements are an index of the developmental status of the general vascular constitution of the patient. There is no correlation between the capacity of the retinal vascular bed and either of the two diseases studied. Contrary to previous impression, no correlation was found between habitus in the kretschmerian sense and the capacity of the vascular bed. (R. M. S.)

Primary Intracranial Sarcomas.—The tumours described have certain features in common. They are of connective tissue nature and must be derived from the leptomeningeal tissue. They are very cellular and contain numerous mitoses. They form scanty intercellular substances characteristic of connective tissue. They spread mainly along the perivascular and leptomeningeal spaces, but may break out of them into the neural parenchyma and then spread diffusely, without forming a capsule. No two of these tumours are ever exactly alike. (R. M. S.)

Serum Protein in Schizophrenia.—Long-term studies of 14 patients with schizophrenia, 11 with manic depressive psychoses, and seven with symptoms of both conditions revealed abnormal variations in the nonprotein nitrogen of the blood and in the total proteins, cholesterol, and fatty acids of the serum in all the persons who showed marked changes in clinical status. The patients whose symptoms showed little change rarely had abnormal variations in these constituents. (R. M. S.)

Histological Changes following Metrazol Convulsions.—Serious lesions were found in the brains of all animals which underwent convulsions from metrazol. Strong evidence of chronic neuropathological lesions, in contrast to changes which might be imputed to lethal seizures only, was observed in animals which had seizures over periods of more than 8 days. The degree and extensiveness of the lesions in these experimental animals corresponded in general with the number and severity of the seizures observed. The type of damage to the brain seemed to be influenced by the length of time during which the animal had seizures. (R. M. S.)

Arrest of Circulation to C.N.S.—Permanent pathological lesions may occur in the cerebral cortex of the cat after complete arrest of the circulation for 3 minutes and 10 seconds. Frank necrosis and softening of the cortex have been observed after circulatory interruption for 3 minutes and 25 seconds.

Circulatory arrest for periods in the neighbourhood of 7½ minutes causes complete destruction and liquefaction necrosis of the cerebral cortex. The motor and visual cortexes sustain the earliest and most profound damage. The olefactory, orbital, and temporal regions of the cortex are the least susceptible. Lamina I and to a lesser extent lamina II are the least vulnerable of the cortical layers, while laminas III and IV are the most vulnerable. The Purkinje cells rank next to the nerve cells of the cerebral cortex in susceptibility. The lateral geniculate nucleus is the most vulnerable of the basal nuclei in the cat, and it is followed, in order of susceptibility, by the hypothalamic nuclei, the thalamic nuclei, the globus pallidus, and the caudate nucleus. The brain stem and spinal cord are uninjured by periods of circulatory arrest compatible with continued survival of the animal. (R. M. S.)

Defects of Memory in Psychoses of Senium.—It was found that in patients suffering from the psychoses of the senium there are a greatly increased tendency to perseverate and a greatly accelerated tendency to secondary elaboration of memorized data. The first process, by interfering primarily with registration, and the second process, by interfering with retention, contribute materially to the improvement of recent memory in these patients. (R. M. S.)

BRAIN

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*Gower's Tract and Spinal Border Cells. S. Cooper and C. S. Sherrington. 123.
*An Experimental Study of the Role of Neurones in the Dissemination of Poliomyelitis Virus in the Nervous System. D. Bodian and H. A. Howe. 135.
*The Relationship Between Amyotonia Congenita and Congenital Myopathy. J. W. Aldren Turner. 163.
*The Tolerance of the Blocked Galenic System against Artificially Increased Intravenous Pressure. B. Schlesinger. 178.
Intracranial Hydatids. C. Langmaid and L. Rogers. 184.
A Study of Cortical Metabolism in Relation to Cerebral Disease. K. C. Dixon. 191.

Gower's Tract.—Chromatolytic changes were observed in large cells resembling motor neurones in the ventro-lateral fringe of the spinal grey matter of the 12th thoracic and upper six lumbo-sacral segments in monkeys and cats, following cord section. The cells, which were most numerous in the 4th and 5th lumbar segments, gave axones which immediately crossed the midline and ascended in the opposite ventro-lateral white matter. This ascending tract is part of Gower's tract, and the authors suggest the name "border cells" for the large cells of origin. (D. J. W.)

Poliomyelitis Virus.—Poliomyelitis virus (Rockefeller M.V.) was introduced into the C.N.S. of sixty Rhesus monkeys via the nose, eye, cortex, cord, and sciatic nerve. The animals were sacrificed in the preparalytic and acute paralytic stages of the disease. The results suggest that the selectivity of the virus is determined by three principal factors—the differential susceptibility of certain areas, their accessibility to an effective concentration, based

upon the kind and quantity of neuronal connection, and the portal of entry, which modifies the second factor. It is possible that immunological processes occurring during the disease enable some cells to survive early sublethal doses. (D. J. W.)

Amytonia Congenita and Congenital Myopathy.—Study of an affected family shows that amyotonia congenita in infancy changes to non-progressive myopathy in adolescence. The clinical picture of amyotonia congenita may be produced either by a congenital myopathy or by a spinal affection related to the Werdnig-Hoffman disease. (D. J. W.)

Blocked Galenic System.—Experimental occlusion of the vein of Galen in adult monkeys did not produce hydrocephalus. (D. J. W.)

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*Studies on Pain. Measurement of the Effect of Morphine, Codeine, and other Opiates on the Pain Threshold and an Analysis of Their Relation to the Pain Experience. H. G. Wolff, J. D. Hardy, and H. Goodell. 659.
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Psychiatric Aspects of Cryptorchidism.—There is no typical personality associated with cryptorchidism, but in a group of 13 true cryptorchids behaviour types were broadly classed as hypokinetic, with mental deficiency or emotional sluggishness, and as hyperkinetic, with instability or conduct disorders. Improvement in mental status or personality could not be correlated in time with descent of the testes under endocrine therapy. (W. M. H.)

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*Effects on Respiration, Blood Pressure, and Gastric Motility of Stimulation of Orbital Surface of Frontal Lobe. P. Bailey and W. H. Sweet. 276.

Micro-Electrodes and Superior Cervical Ganglion.—Micro-electrodes in the superior cervical ganglion of the cat or rabbit show on preganglionic stimulation axon-like spikes. Their brief duration and sharp localization and all-or-none character suggest they come from single cells. Latency varies considerably. Frequency of response may be independent of the stimuli. The spike is followed by one negative and two positive after potentials, the last coinciding with the slow after potential of the ganglionic record. (W. M. H.)

Pupillary Reactions in Cortical Lesions.—Ablation of the sensory or sensorimotor cortex does not raise the threshold to pain reaction, the indicator being reflex dilation of the pupil caused by inhibition of the Edinger Westphal nucleus. Massive cortical lesions lower the threshold. Cortical areas which inhibit extrapyramidal movements produce dilation of the sympathectomized pupil. A cortical control by inhibition is indicated. (W. M. H.)

Postural Reflexes in Infants.—A study of 100 healthy, newborn premature and full-term infants showed a definite effect of head posture in relation to trunk upon grasping movements. The latter are not necessarily a part of the tonic neck reflex mechanism. The relationship was shown between the position of the body in space and reflex postures in the limbs or toes. (W. M. H.)

Ether and Nembutal Action on Nervous System.—A full report, too lengthy to summarize, on the action of these drugs on potential responses of the nerve axon, synapse, rhythmically active nerve cell, spinal cord and brain. (W. M. H.)

Motor Performance after Parietal Ablation.—Unilateral removal of the parietal lobe, like ablations of areas 6 or 4, causes disability with relative disuse of the operated extremity and greater involvement of the distal joints. However, accuracy of control is increased by focused visual attention ; in emotion control of gross movements may be almost perfect. Tactile deficit following unilateral or partial ablations of either areas 3.1.2, 1.2, or 5 and 7 is shown in the placing and hopping responses. Proprioception is much less affected, but complete bilateral parietal removal abolished the hopping and tactile and proprioceptive placing reactions. Knee-jerks, at first absent, may become hyperactive. Resistance to manipulation remains diminished. Atrophy of muscles was noted in one case. (W. M. H.)

Reflexes in Spinal Monkeys.—After spinal transection in the monkey autonomic functions return more slowly than somatic reflexes and fail to return to their normal efficiency. Cooling of one limb fails to cause a drop in temperature in the other during the period of " shock " following transection. (W. M. H.)

Effects of Stimulation of Frontal Lobe.—In both cats and monkeys an area on the orbital surface inhibits respiration and gastric tonus and causes a rise in blood pressure. The latter effect is found especially in monkeys. In cats the inhibition of tonus in gastric muscles is less frequent. (W. M. H.)

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Sympathominetic Amines and Perfused Blood Vessels.—The vasoconstrictor effect of sympathomimetic amines was determined by perfusion of cat's hind legs. Amines with hydroxyl groups in the ortho- or para- position and with unsubstituted phenyl ring are largely dependent for their effect on the presence of adrenaline. It is suggested they may block local tissue mechanisms for the inactivation of adrenaline. Dihydroxy- and meta-hydroxy- compounds appear to act independently. (W. M. H.)

Inactivation of Adrenaline.—d- and l-adrenaline, epinine, and corbasil, a derivative of ephedrine, given by mouth are

eliminated in the form of conjugated derivatives in the urine. Epinine and adrenaline are not eliminated to any extent as protocatechuic acid, as would be expected if inactivation were by the amine oxidase. Oxidation of adrenaline given by mouth (in doses up to 30 mg.) is prevented by adding 1 per cent. acetic acid along with glycine. (W. M. H.)

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BOOK REVIEWS

PSYCHOLOGICAL STUDIES IN DEMENTIA PRÆCOX

I. Kendig and W. V. Richmond

(Edwards Bros. Inc., Ann Arbor, Michigan, U.S.A. 1940.)

This is an extensive analysis of the intelligence test results (Stanford-Binet) accumulated during the previous 15 years in the ordinary clinical use of this test at the St. Elizabeth's Hospital, Washington, U.S.A. The author compared the 500 dementia præcox cases tested during this period with several other types of psychosis and with two groups of normals comprising together 346 individuals. Their main conclusion is that this test demonstrates some intellectual impairment in dementia præcox ; they add that it may be merely functional impairment. They have also reviewed and compared the conflicting evidence already published bearing on this problem of the influence of this psychosis on intelligence. They have analysed their results in many ways, calculated a general mental age, vocabulary age, efficiency index, and also assessed the school achievements of their patients, the age of onset of their psychosis, and repeated the test 10 years later with those patients still in hospital and testable (41). With very few exceptions the findings in these repeated tests showed no fall and often a slight rise in mental age—after a period during which the clinical picture had deteriorated. Seeing that the tests had only been performed on those cases in whom the clinician had thought the test might be relevant, an undue proportion of cases with low innate intelligence might well have been included in their group. Their analysis of the pattern of the test results shows no type of response to be characteristic of this psychosis. Should this study be complemented by a further small group of completely unselected cases of dementia præcox similarly tested, to determine the general level of mental age, all interested in this problem would welcome this as a comprehensive assessment of the findings of this test in dementia præcox.

HOPOUSIA, OR THE SEXUAL AND ECONOMIC FOUNDATION OF A NEW SOCIETY

J. D. Unwin

(George Allen and Unwin, Ltd., London. 1940. Pp. 475. 21*s*.)

The late J. D. Unwin showed in his book " Sex and Culture " that he had the rare ability to formulate general principles covering a great mass of seemingly confused data. In this posthumous work he has carried further some ideas implicit in his earlier book, in which he held the manifestations of increased energy in human society to be the effect of enforced sexual continence, and he has sought to describe the structure of a society (Hopousia) organized to display the greatest possible energy. The argument, though in places left incomplete because of his untimely death, is lucidly and cogently stated, and is typical of Unwin's wide-ranging, penetrating, and original mind. It deals largely with economic and political questions, and cannot be briefly summarized.

MYTHOLOGY OF THE SOUL

H. G. Baynes

(Baillière, Tindall and Cox, London. 1940. Pp. 939. 32*s.* 6*d.*)

Dr. Baynes here interprets the drawings and dreams of two patients whom he treated for a psychopathic condition, regarded by him as borderline schizophrenia. The correctness of this diagnosis is open to question, but those who question it are likely to consider the diagnosis as a minor point in comparison with the method and psychopathology used.

Dr. Baynes has deliberately turned away from what he describes as " the extraverted quantitative approach which seeks to accumulate facts, without much concern for their meaning," and he holds that for the investigation of fundamental psychological problems " only an introverting psychological method is suitable." Dr. Baynes has a vast respect for Professor Jung of Zurich, whose analytical method he calls the only effective introverting technique in the West to-day—" of the introverted way C. G. Jung is our single source and our sole tradition."

From this it follows that the reader's appreciation of the book will depend on whether he can accept whole-heartedly Jung's mythological interpretation of mental happenings. The book is diffuse, esoteric, and very long. It contains many speculations that are ingenious and far-fetched. The second of the two patients had much artistic ability, evident in the many drawings and paintings reproduced.

THE NEUROGENIC BLADDER

F. C. McLellan

(Baillière, Tindall and Cox, London. 1940. Pp. 206. 22*s.*)

Glancing at the title the conventional student of the mother tongue must get a jolt, but if he is an urologist as well he will appreciate a review of some importance on perusing the appropriately straw-coloured pages of this well-bound volume. It is designed to give the student or diagnostician a résumé of the anatomy and physiology of the bladder and instruction in the methods of cystometry. These are discussed in the light of findings in two hundred cases of disorder of bladder function. The features in half that number are tabulated and there are numerous charts of cystometric studies, standardized and readily understood. On the whole the author's correlation of clinical findings and the facts of experimental physiology is adequate. The general classification of disorders of the bladder is acceptable, save perhaps again for an unhappy nomenclature. It is based on the nature of the defect in the reflex mechanism of the bladder. The views expressed on the role of the sympathetic innervation are debatable. From experiments with irritative solutions and electrical stimulation in a subject with a cauda equina lesion and intact sympathetic supply he concludes that " the thoraco-lumbar sympathetic fibres carry no afferent sensory components from the bladder." He considers that in such cases awareness of distension may be due to disturbances in the surrounding organs. In the face of suggestive data in some of his own cases he takes the view that " visceral sensations of distension and contraction have not been proved to be transmitted by sympathetic fibres." To the reviewer the work of Talaat on the mediation of impulses, provoked by overdistension, in slowly adapting fibres of the hypogastrics would seem worthy of citation. While views on such points may vary, most readers will concur that this volume must forward the use of cystometry in neurological studies. Inconsistencies in spelling and errors in numbering of references demand a measure of that forgiveness for errors entreated in the author's preface.

THE HISTAMINE AND INSULIN TREATMENT OF SCHIZOPHRENIA AND OTHER MENTAL DISEASES

Horace Hill

(Baillière, Tindall and Cox, London. 1940. Pp. 133. 6*s*.)

This is an unconvincing account of the author's procedure in the treatment of schizophrenics. He has combined histamine with insulin because he assumes that in any so-called " shock " treatment histamine is the effective agent. The naïveté of this is in keeping with the tone of the whole book, which is as weak on the psychiatric as on the pharmacological side. Records of cures and improved cases are included.

INJURIES OF THE SKULL, BRAIN, AND SPINAL CORD

Edited by Samuel Brock

(Baillière, Tindall and Cox, London. 1940. Pp. 632. 32*s*. 6*d*.)

During a period when injuries affecting the nervous system have greatly increased in number, it is of inestimable value to have in compact form the expression of opinion of authorities on the many-sided aspects of such injuries. As is always so in a book of many authors, there is considerable overlap in the matter and further a tendency to a lack of exactness in terminology. But such deficiencies are amply off-set by the wealth of useful exposition. The chapter devoted to concussion and contusion is most welcome as giving a very clear picture of the varying states found in such conditions and more especially the changes exhibited by a patient recovering from one or other. In the chapter given over to post-traumatic epilepsy a very complete survey of the literature on the subject is presented, along with the author's experience in a large number of personally observed cases. Following an excellent chapter on injuries of the spinal cord and nerve roots, there is a short one on the relationship of spinal cord injuries to other diseases of the spinal cord : the possible association is of such importance in medico-legal matters that it is disappointing not to have more space and information given to this aspect of injuries. Over a hundred pages are devoted to the neuroses, psychotic states, and simulation symptoms following head injury : these are the pages which are most likely to be criticized, not so much for the detail, but rather for the tendency to over-classification. Although mention has been made of only these few chapters, it is not to be assumed that the many others do not contain much of value.

The book, well printed and remarkably free from printers' errors, is one of the most useful additions to the literature on injuries of the nervous system. It is to be commended to all who may be concerned with the management of cases of head and spinal injuries.

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